```
=> d his ful

     (FILE 'HOME' ENTERED AT 15:41:34 ON 31 JUL 2006)

     FILE 'REGISTRY' ENTERED AT 15:41:43 ON 31 JUL 2006
L1             STR
L2           4 SEA SSS SAM L1
L3         129 SEA SSS FUL L1

     FILE 'HCAPLUS' ENTERED AT 15:45:14 ON 31 JUL 2006
               E US2003-656059/APPS
L4           1 SEA ABB=ON  PLU=ON  US2003-656059/AP
L5           3 SEA ABB=ON  PLU=ON  L3
L6           1 SEA ABB=ON  PLU=ON  L4 AND L5
               D L4 IBIB
               E CAI H/AU
L7         252 SEA ABB=ON  PLU=ON  ("CAI H"/AU OR "CAI H B"/AU OR "CAI H
               F"/AU OR "CAI H J"/AU OR "CAI H L"/AU OR "CAI H N"/AU OR "CAI
               H T"/AU OR "CAI H W"/AU OR "CAI H Y"/AU OR "CAI H Z"/AU OR
               "CAI HUI"/AU OR "CAI HUI CONG"/AU OR "CAI HUI GUO"/AU OR "CAI
               HUI JUAN"/AU OR "CAI HUI LIN"/AU OR "CAI HUI LUO"/AU OR "CAI
               HUI MIN"/AU OR "CAI HUI MING"/AU OR "CAI HUI NONG"/AU OR "CAI
               HUI QUAN"/AU OR "CAI HUI QUN"/AU OR "CAI HUI RU"/AU OR "CAI
               HUI WEI"/AU OR "CAI HUI WU"/AU OR "CAI HUI XIA"/AU OR "CAI HUI
               YAN"/AU OR "CAI HUI YUN"/AU OR "CAI HUI ZHEN"/AU OR "CAI HUI
               ZHI"/AU)
               E CARRUTHERS N/AU
L8          91 SEA ABB=ON  PLU=ON  ("CARRUTHERS N"/AU OR "CARRUTHERS N I"/AU
               OR "CARRUTHERS NIALL"/AU OR "CARRUTHERS NICHOLAS"/AU OR
               "CARRUTHERS NICHOLAS I"/AU OR "CARRUTHERS NICHOLAS IAIN"/AU OR
               "CARRUTHERS NICHOLAS J"/AU OR "CARRUTHERS NICK"/AU OR "CARRUTHE
               RS NICOLAS IAIN"/AU)
               E DVORAK C/AU
L9          29 SEA ABB=ON  PLU=ON  "DVORAK C"/AU OR "DVORAK CURT A"/AU
               E EDWARDS J/AU
L10        368 SEA ABB=ON  PLU=ON  ("EDWARDS J"/AU OR "EDWARDS J P"/AU OR
               "EDWARDS J P N"/AU OR "EDWARDS JAMES"/AU OR "EDWARDS JAMES
               P"/AU OR "EDWARDS JAMES PATRICK"/AU)
               E KWOK A/AU
L11         21 SEA ABB=ON  PLU=ON  ("KWOK A"/AU OR "KWOK A K"/AU OR "KWOK
               ANNETTE"/AU OR "KWOK ANNETTE K"/AU)
L12         31 SEA ABB=ON  PLU=ON  (L7 AND (L8 OR L9 OR L10 OR L11)) OR (L8
               AND (L9 OR L10 OR L11)) OR (L9 AND (L10 OR L11)) OR (L10 AND
               L11)
L13        713 SEA ABB=ON  PLU=ON  (L7 OR L8 OR L9 OR L10 OR L11)
L14          2 SEA ABB=ON  PLU=ON  L13 AND (L3 OR HETERCYCL?/TI)
L15         31 SEA ABB=ON  PLU=ON  L12 OR L14
               D QUE
               D L15 IBIB ABS 1-31

     FILE 'BEILSTEIN' ENTERED AT 15:55:13 ON 31 JUL 2006
L16          0 SEA SSS FUL L1

     FILE 'MARPAT' ENTERED AT 15:55:31 ON 31 JUL 2006
L17          0 SEA SSS SAM L1
L18          2 SEA SSS FUL L1
L19          1 SEA ABB=ON  PLU=ON  L18/COM
L20          0 SEA ABB=ON  PLU=ON  L19 NOT L5
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FILE HOME

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 30 JUL 2006 HIGHEST RN 897385-07-8
DICTIONARY FILE UPDATES: 30 JUL 2006 HIGHEST RN 897385-07-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 31 Jul 2006 VOL 145 ISS 6
FILE LAST UPDATED: 30 Jul 2006 (20060730/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BEILSTEIN
FILE LAST UPDATED ON JUNE 16, 2006

FILE COVERS 1771 TO 2006.
FILE CONTAINS 9,606,495 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link

between a BEILSTEIN compound and belonging reactions. For mo
detailed reaction searches BRNs can be searched as reaction
partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

****
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
* FOR PRICE INFORMATION SEE HELP COST *
****

NEW

* ***PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.***
* ***NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.***

FILE MARPAT
FILE CONTENT: 1961-PRESENT VOL 145 ISS 5 (20060728/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 2006135764 22 JUN 2006
DE 102004055316 18 MAY 2006
EP 1674464 28 JUN 2006
JP 2006128031 18 MAY 2006
WO 2006058720 08 JUN 2006
GB 2419594 03 MAY 2006
FR 2877945 19 MAY 2006
RU 2276150 10 MAY 2006
CA 2518664 10 MAR 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

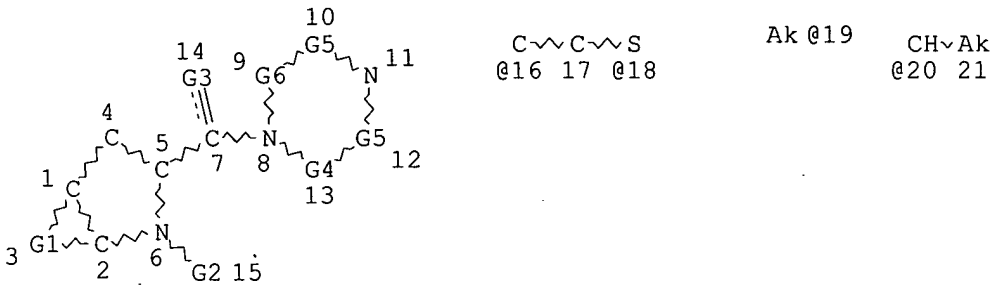
=> fil hcap
FILE 'HCAPLUS' ENTERED AT 15:56:11 ON 31 JUL 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 31 Jul 2006 VOL 145 ISS 6
FILE LAST UPDATED: 30 Jul 2006 (20060730/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que l5
L1 STR



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VAR G2=H/19
VAR G3=O/S
VAR G4=CH2/20
REP G5=(1-2) CH
VAR G6=CH2/22
NODE ATTRIBUTES:
NSPEC IS RC AT 23
CONNECT IS E1 RC AT 19
CONNECT IS E1 RC AT 21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
L3 129 SEA FILE=REGISTRY SSS FUL L1
L5 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

=> d l5 ibib abs hitstr 1-3

L5 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1250889 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 144:128937
TITLE: Preparation and Biological Evaluation of Indole, Benzimidazole, and Thienopyrrole Piperazine

Carboxamides: Potent Human Histamine H4 Antagonists

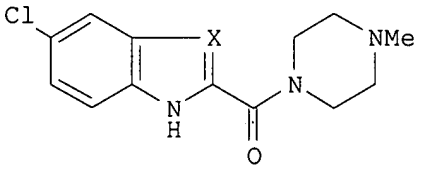
AUTHOR(S): Venable, Jennifer D.; Cai, Hui; Chai, Wenying; Dvorak, Curt A.; Grice, Cheryl A.; Jablonowski, Jill A.; Shah, Chandra R.; Kwok, Annette K.; Ly, Kiev S.; Pio, Barbara; Wei, Jianmei; Desai, Pragnya J.; Jiang, Wen; Nguyen, Steven; Ling, Ping; Wilson, Sandy J.; Dunford, Paul J.; Thurmond, Robin L.; Lovenberg, Timothy W.; Karlsson, Lars; Carruthers, Nicholas I.; Edwards, James P.

CORPORATE SOURCE: Johnson Johnson Pharmaceutical Research and Development L.L.C., San Diego, CA, 92121, USA

SOURCE: Journal of Medicinal Chemistry (2005), 48(26), 8289-8298
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



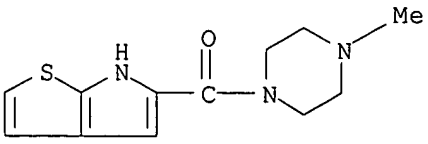
I

AB Three series of H4 receptor ligands, derived from indoly-2-yl-(4-methyl-piperazin-1-yl)methanones, have been synthesized and their structure-activity relationships evaluated for activity at the H4 receptor in competitive binding and functional assays. In all cases, substitution of small lipophilic groups in the 4 and 5-positions led to increased activity in a [3H]histamine radiolabeled ligand competitive binding assay. In vitro metabolism and initial pharmacokinetic studies were performed on selected compds. leading to the identification of carboxamides I [X = CH, N] as potent H4 antagonists with the potential for further development. In addition, I demonstrated efficacy in in vitro mast cell and eosinophil chemotaxis assays.

IT ***668479-93-4P 668479-96-7P 668480-03-3P 668480-09-9P 668480-14-6P 668480-32-8P***
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of benzimidazolecarbonyl-, thienopyrrolecarbonyl-, and indolecarbonylpiperazines as human histamine H4 antagonists)

RN 668479-93-4 HCAPLUS

CN Piperazine, 1-methyl-4-(6H-thieno[2,3-b]pyrrol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



RN 668479-96-7 HCAPLUS
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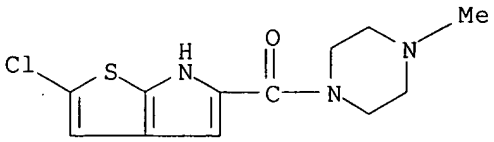
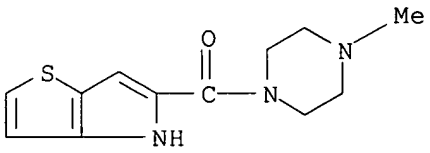
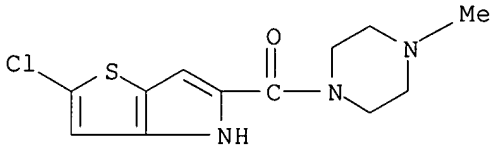


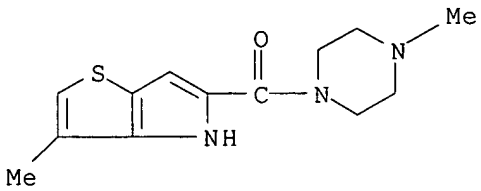
RN 668480-03-3 HCAPLUS
CN Piperazine, 1-methyl-4-(4H-thieno[3,2-b]pyrrol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



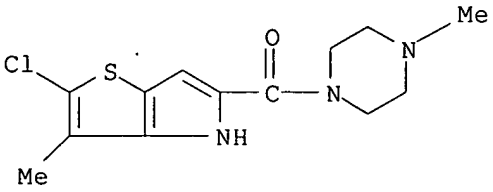
RN 668480-09-9 HCAPLUS
CN Piperazine, 1-[(2-chloro-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 668480-14-6 HCAPLUS
CN Piperazine, 1-methyl-4-[(3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



RN 668480-32-8 HCAPLUS
CN Piperazine, 1-[(2-chloro-3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:220164 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 140:247611
TITLE: Identification of histamine H4 receptor modulators and uses thereof for the treatment of allergy and asthma
INVENTOR(S): Desai, Pragnya J.; Dunford, Paul J.; Hofstra, Claudia L.; Karlsson, Lars; Leung, Wai-ping; Ling, Ping; Thurmond, Robin L.
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004021999	A2	20040318	WO 2003-US27943		20030905
WO 2004021999	A3	20041007			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2497788	AA	20040318	CA 2003-2497788		20030905
AU 2003265961	A1	20040329	AU 2003-265961		20030905
US 2004127395	A1	20040701	US 2003-656385		20030905
EP 1545596	A2	20050629	EP 2003-794649		20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2006510590	T2	20060330	JP 2004-534688		20030905
PRIORITY APPLN. INFO.:			US 2002-408736P	P	20020906
			US 2002-408569P	P	20020906
			US 2002-408579P	P	20020906
			WO 2003-US27943	W	20030905

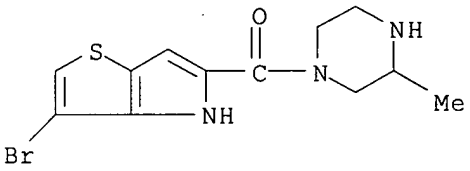
AB Methods are disclosed for identifying histamine receptor modulators that affect mast cell or basophil chemotaxis, and the use of such histamine H4 receptor modulators for the prevention, treatment, induction, or other desired modulation of asthma and/or allergic responses, or diseases and/or

conditions that are modulated, affected or caused by asthma or allergic responses. Also disclosed is the use of histamine H4 receptor modulators for the prevention, treatment, induction, or other desired modulation of mast cell or basophil chemotactic responses, such as migration to a particular site, or diseases and/or conditions that are modulated, affected or caused by mast cell or basophil chemotaxis.

IT ***668480-27-1***
RL: BSU (Biological study, unclassified); BIOL (Biological study) (binding affinity to H4 receptor, effect on H4 receptor-mediated mast cell chemotaxis; identification of histamine H4 receptor modulators and uses thereof for treatment of allergy and asthma)

RN 668480-27-1 HCAPLUS

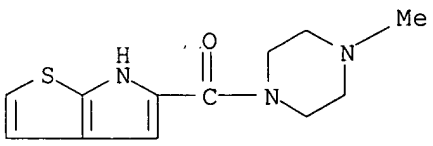
CN Piperazine, 1-[(3-bromo-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-3-methyl- (9CI) (CA INDEX NAME)



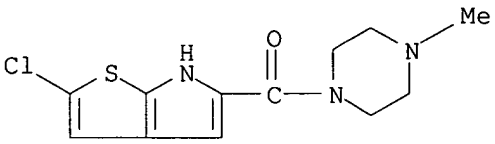
IT ***668479-93-4***, (4-Methylpiperazin-1-yl)(6H-thieno[2,3-b]pyrrol-5-yl)methanone ***668479-96-7***, (2-Chloro-6H-thieno[2,3-b]pyrrol-5-yl)(4-methylpiperazin-1-yl)methanone ***668479-98-9*** ***668479-99-0***, (2-Chloro-6H-thieno[2,3-b]pyrrol-5-yl)piperazin-1-ylmethanone ***668480-03-3***, (4-Methylpiperazin-1-yl)(4H-thieno[3,2-b]pyrrol-5-yl)methanone ***668480-09-9***, (2-Chloro-4H-thieno[3,2-b]pyrrol-5-yl)(4-methylpiperazin-1-yl)methanone ***668480-12-4***, (3-Bromo-4H-thieno[3,2-b]pyrrol-5-yl)(4-methylpiperazin-1-yl)methanone ***668480-14-6***, (4-Methylpiperazin-1-yl)(3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)methanone ***668480-20-4***, (2,3-Dimethyl-4H-thieno[3,2-b]pyrrol-5-yl)(4-methylpiperazin-1-yl)methanone ***668480-22-6*** ***668480-28-2***, (3-Methyl-4H-thieno[3,2-b]pyrrol-5-yl)piperazin-1-ylmethanone ***668480-30-6*** ***668480-32-8***, (2-Chloro-3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)(4-methylpiperazin-1-yl)methanone ***668480-33-9***, (2-Chloro-3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)piperazin-1-ylmethanone ***668480-35-1***, (2,3-Dichloro-4H-thieno[3,2-b]pyrrol-5-yl)(4-methylpiperazin-1-yl)methanone
RL: BSU (Biological study, unclassified); BIOL (Biological study) (binding affinity to H4 receptor; identification of histamine H4 receptor modulators and uses thereof for treatment of allergy and asthma)

RN 668479-93-4 HCAPLUS

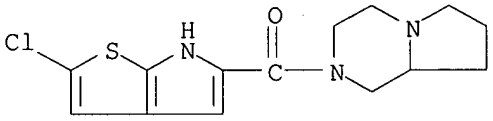
CN Piperazine, 1-methyl-4-(6H-thieno[2,3-b]pyrrol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



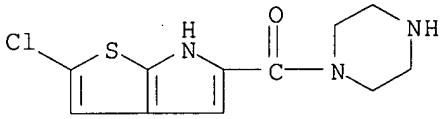
RN 668479-96-7 HCAPLUS
CN Piperazine, 1-[(2-chloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 668479-98-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine, 2-[(2-chloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]octahydro- (9CI) (CA INDEX NAME)



RN 668479-99-0 HCAPLUS
CN Piperazine, 1-[(2-chloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



RN 668480-03-3 HCAPLUS
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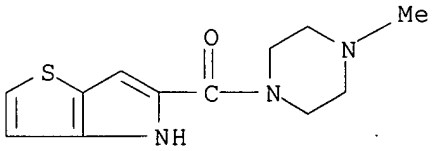
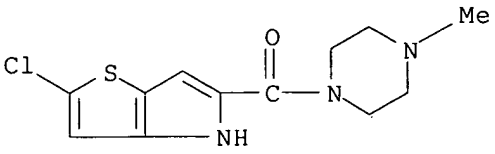


RN 668480-09-9 HCAPLUS
CN Piperazine, 1-[(2-chloro-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 668480-12-4 HCAPLUS
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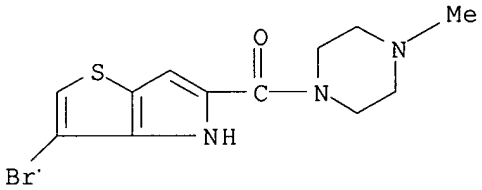
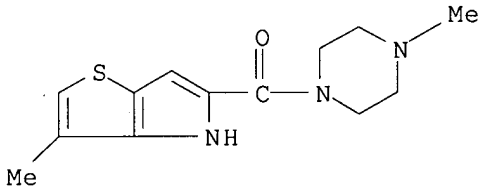
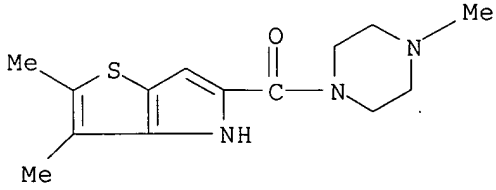


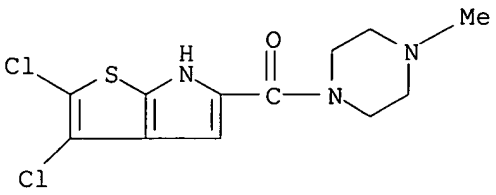
RN 668480-14-6 HCAPLUS
CN Piperazine, 1-methyl-4-[(3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



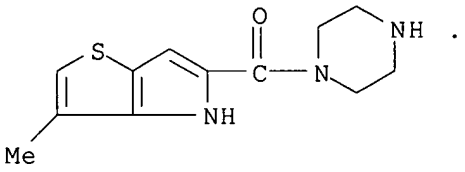
RN 668480-20-4 HCAPLUS
CN Piperazine, 1-[(2,3-dimethyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



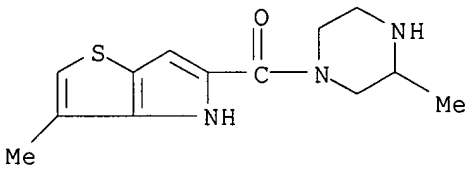
RN 668480-22-6 HCAPLUS
CN Piperazine, 1-[(2,3-dichloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



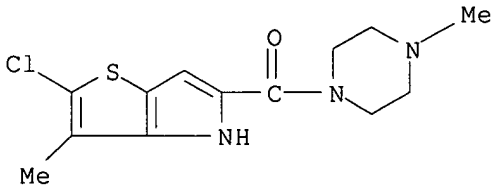
RN 668480-28-2 HCAPLUS
CN Piperazine, 1-[(3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



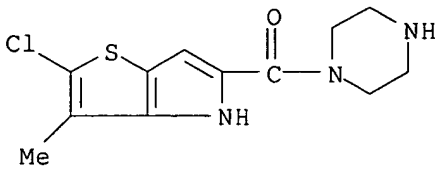
RN 668480-30-6 HCAPLUS
CN Piperazine, 3-methyl-1-[(3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



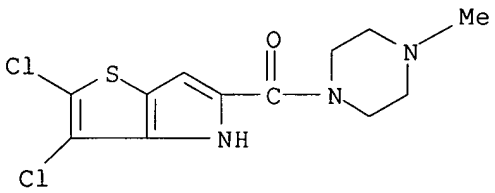
RN 668480-32-8 HCAPLUS
CN Piperazine, 1-[(2-chloro-3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 668480-33-9 HCAPLUS
CN Piperazine, 1-[(2-chloro-3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



RN 668480-35-1 HCAPLUS
CN Piperazine, 1-[(2,3-dichloro-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:203556 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 140:235696
TITLE: Preparation of piperazinecarbonyl heterocyclic compounds as histamine H4 antagonists
INVENTOR(S): Cai, Hui; Carruthers, Nicholas I.; Dvorak, Curt A.; Edwards, James P.; Kwok, Annette K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004048878	A1	20040311	US 2003-656059	20030905
CA 2497868	AA	20040318	CA 2003-2497868	20030905
WO 2004022537	A2	20040318	WO 2003-US28017	20030905
WO 2004022537	A3	20040506		
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EP 1543011	A2	20050622	EP 2003-754461	20030905
EP 1543011	B1	20060503		

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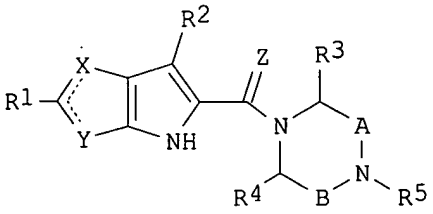
JP 2006500394 T2 20060105 JP 2004-534722 20030905
PRIORITY APPLN. INFO.: US 2002-408723P P 20020906
WO 2003-US28017 W 20030905
OTHER SOURCE(S): MARPAT 140:235696

GI



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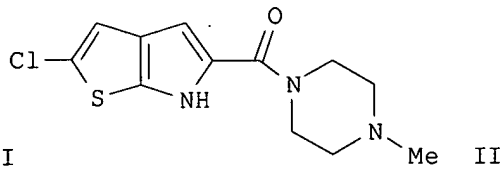
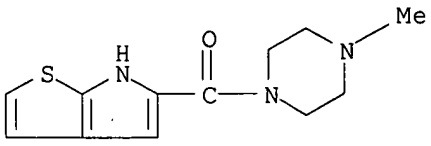


II

AB Thienopyrrolyl and furanopyrrolyl compds. of formula I [X, Y = CR6, O, S; Z = O, S; R1, R6 = H, halo, alkyl, alkoxy, etc.; R2 = H, halo, alkyl; R3, R4 = H, alkyl, cycloalkyl, etc.; R5 = H, CN, alkyl, etc.; A = (substituted) (CH2)m; B = (substituted) (CH2)n; m, n = 1-2; AR5 = alkylene, heteroalkylene] are prepared which are useful to treat or prevent disorders and conditions mediated by the histamine H4 receptor, including allergic rhinitis. Thus, II was prepared by annulation of thiophene-3-carboxaldehyde and Et azidoacetate, hydrolysis, reaction with N-chlorosuccinimide, then amidation with N-methylpiperazine. The Ki value of II was 25 nM against human histamine H4 receptor.

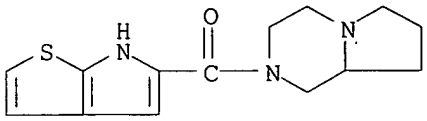
IT ***668479-93-4P 668479-94-5P 668479-96-7P***
668479-98-9P 668479-99-0P 668480-03-3P
668480-05-5P 668480-07-7P 668480-09-9P
668480-10-2P 668480-12-4P 668480-14-6P
668480-20-4P 668480-22-6P 668480-25-9P
668480-27-1P 668480-28-2P 668480-30-6P
668480-32-8P 668480-33-9P 668480-35-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinecarbonyl heterocyclic compds. as histamine H4 antagonists)

RN 668479-93-4 HCAPLUS
CN Piperazine, 1-methyl-4-(6H-thieno[2,3-b]pyrrol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)

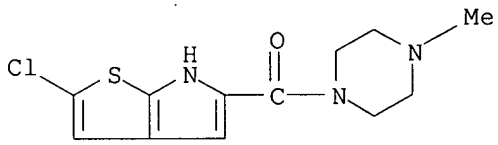


RN 668479-94-5 HCAPLUS

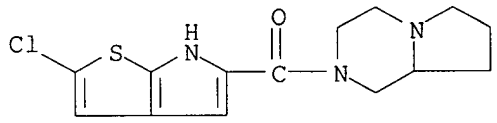
CN Pyrrolo[1,2-a]pyrazine, octahydro-2-(6H-thieno[2,3-b]pyrrol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



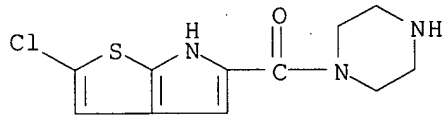
RN 668479-96-7 HCAPLUS
CN Piperazine, 1-[(2-chloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



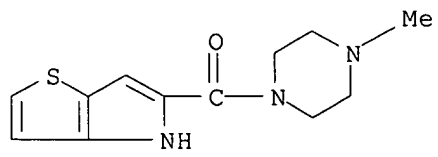
RN 668479-98-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine, 2-[(2-chloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]octahydro- (9CI) (CA INDEX NAME)



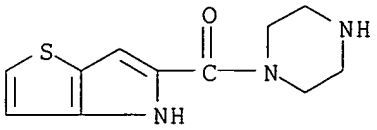
RN 668479-99-0 HCAPLUS
CN Piperazine, 1-[(2-chloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



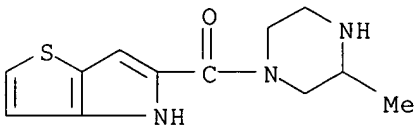
RN 668480-03-3 HCAPLUS
CN Piperazine, 1-methyl-4-(4H-thieno[3,2-b]pyrrol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



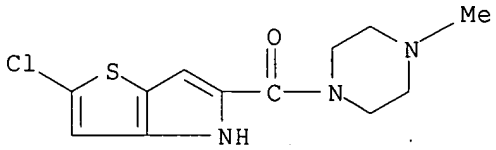
RN 668480-05-5 HCAPLUS
CN Piperazine, 1-(4H-thieno[3,2-b]pyrrol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



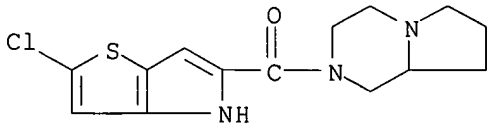
RN 668480-07-7 HCAPLUS
CN Piperazine, 3-methyl-1-(4H-thieno[3,2-b]pyrrol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



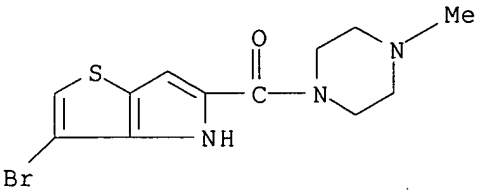
RN 668480-09-9 HCAPLUS
CN Piperazine, 1-[(2-chloro-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 668480-10-2 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine, 2-[(2-chloro-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]octahydro- (9CI) (CA INDEX NAME)



RN 668480-12-4 HCAPLUS
CN Piperazine, 1-[(3-bromo-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



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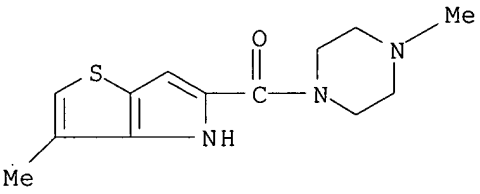
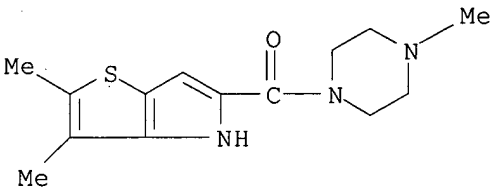
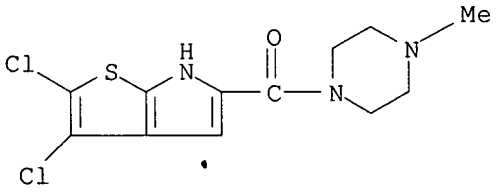
CN Piperazine, 1-methyl-4-[(3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



RN 668480-20-4 HCAPLUS
CN Piperazine, 1-[(2,3-dimethyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 668480-22-6 HCAPLUS
CN Piperazine, 1-[(2,3-dichloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 668480-25-9 HCAPLUS
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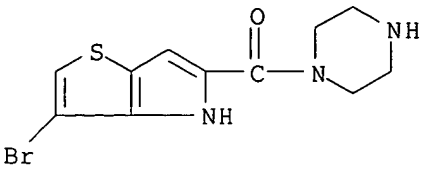
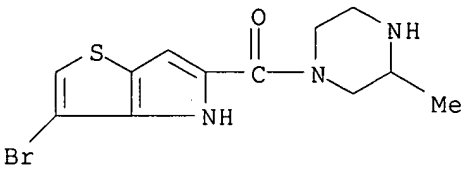
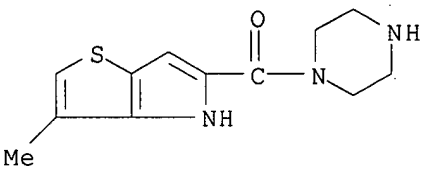


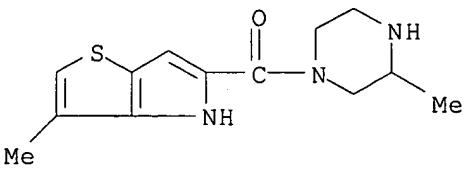
RN 668480-27-1 HCAPLUS
CN Piperazine, 1-[(3-bromo-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]-3-methyl- (9CI) (CA INDEX NAME)



RN 668480-28-2 HCAPLUS
CN Piperazine, 1-[(3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



RN 668480-30-6 HCAPLUS
CN Piperazine, 3-methyl-1-[(3-methyl-4H-thieno[3,2-b]pyrrol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



RN 668480-32-8 HCAPLUS
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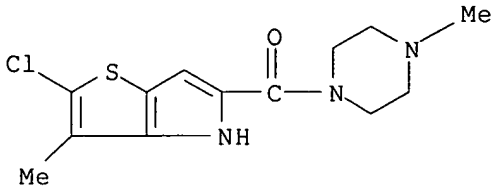

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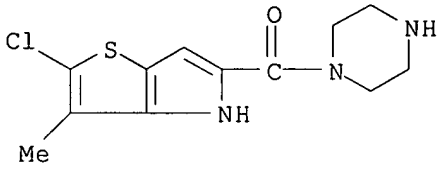

RN 668480-35-1 HCAPLUS
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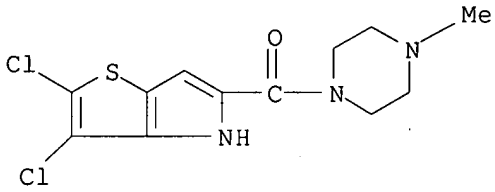

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L15         31 L12 OR L14

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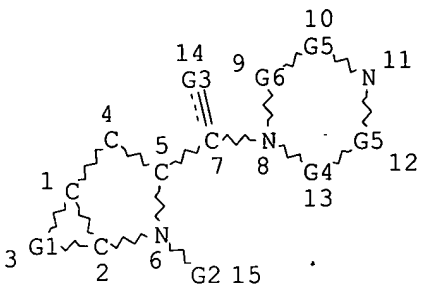

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Ak @19

CH~Ak
@20 21

CH~C
@22 23

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VAR G2=H/19
VAR G3=O/S
VAR G4=CH2/20
REP G5=(1-2) CH
VAR G6=CH2/22
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CONNECT IS E1  RC AT  19
CONNECT IS E1  RC AT  21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  23

STEREO ATTRIBUTES: NONE
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                H Z"/AU OR "CAI HUI"/AU OR "CAI HUI CONG"/AU OR "CAI HUI
                GUO"/AU OR "CAI HUI JUAN"/AU OR "CAI HUI LIN"/AU OR "CAI HUI
                LUO"/AU OR "CAI HUI MIN"/AU OR "CAI HUI MING"/AU OR "CAI HUI
                NONG"/AU OR "CAI HUI QUAN"/AU OR "CAI HUI QUN"/AU OR "CAI HUI
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                XIA"/AU OR "CAI HUI YAN"/AU OR "CAI HUI YUN"/AU OR "CAI HUI
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                NICHOLAS"/AU OR "CARRUTHERS NICHOLAS I"/AU OR "CARRUTHERS
                NICHOLAS IAIN"/AU OR "CARRUTHERS NICHOLAS J"/AU OR "CARRUTHERS
                NICK"/AU OR "CARRUTHERS NICOLAS IAIN"/AU)
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L9 29 SEA FILE=HCAPLUS ABB=ON PLU=ON "DVORAK C"/AU OR "DVORAK CURT A"/AU
L10 368 SEA FILE=HCAPLUS ABB=ON PLU=ON ("EDWARDS J"/AU OR "EDWARDS J P"/AU OR "EDWARDS J P N"/AU OR "EDWARDS JAMES"/AU OR "EDWARDS JAMES P"/AU OR "EDWARDS JAMES PATRICK"/AU)
L11 21 SEA FILE=HCAPLUS ABB=ON PLU=ON ("KWOK A"/AU OR "KWOK A K"/AU OR "KWOK ANNETTE"/AU OR "KWOK ANNETTE K"/AU)
L12 31 SEA FILE=HCAPLUS ABB=ON PLU=ON (L7 AND (L8 OR L9 OR L10 OR L11)) OR (L8 AND (L9 OR L10 OR L11)) OR (L9 AND (L10 OR L11)) OR (L10 AND L11)
L13 713 SEA FILE=HCAPLUS ABB=ON PLU=ON (L7 OR L8 OR L9 OR L10 OR L11)
L14 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND (L3 OR HETERCYCL?/TI)

L15 31 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 OR L14

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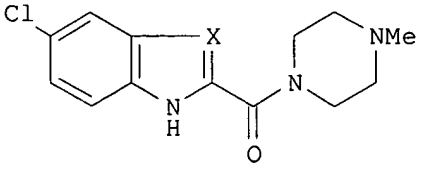
L15 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1250889 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 144:128937
TITLE: Preparation and Biological Evaluation of Indole, Benzimidazole, and Thienopyrrole Piperazine Carboxamides: Potent Human Histamine H4 Antagonists
AUTHOR(S): Venable, Jennifer D.; ***Cai, Hui***; Chai, Wenying; ***Dvorak, Curt A.***; Grice, Cheryl A.; Jablonowski, Jill A.; Shah, Chandra R.; ***Kwok, Annette K.***; Ly, Kiev S.; Pio, Barbara; Wei, Jianmei; Desai, Pragnya J.; Jiang, Wen; Nguyen, Steven; Ling, Ping; Wilson, Sandy J.; Dunford, Paul J.; Thurmond, Robin L.; Lovenberg, Timothy W.; Karlsson, Lars; ***Carruthers, Nicholas I.***; ***Edwards, James P.***
CORPORATE SOURCE: Johnson Johnson Pharmaceutical Research and Development L.L.C., San Diego, CA, 92121, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(26), 8289-8298
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Three series of H4 receptor ligands, derived from indoly-2-yl-(4-methyl-piperazin-1-yl)methanones, have been synthesized and their structure-activity relationships evaluated for activity at the H4 receptor in competitive binding and functional assays. In all cases, substitution

of small lipophilic groups in the 4 and 5-positions led to increased activity in a [3H]histamine radiolabeled ligand competitive binding assay. In vitro metabolism and initial pharmacokinetic studies were performed on selected compds. leading to the identification of carboxamides I [X = CH, N] as potent H4 antagonists with the potential for further development. In addition, I demonstrated efficacy in in vitro mast cell and eosinophil chemotaxis assays.

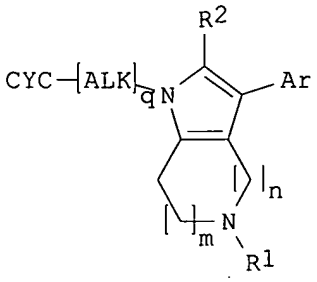
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:395314 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 142:447211
TITLE: Preparation of fused heterocyclic compounds as serotonin modulators
INVENTOR(S): ***Carruthers, Nicholas I.***; Chai, Wenying; Deng, Xiaohu; ***Dvorak, Curt A.***; ***Kwok, Annette K.***; Liang, Jimmy T.; Mani, Neelakandha; Rudolph, Dale A.; Wong, Victoria D.
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N. V., Belg.
SOURCE: PCT Int. Appl., 323 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005040169	A2	20050506	WO 2004-US30190	20040915
WO 2005040169	A3	20060330		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004283196	A1	20050506	AU 2004-283196	20040915
CA 2539426	AA	20050506	CA 2004-2539426	20040915
US 2005119295	A1	20050602	US 2004-941664	20040915
EP 1668014	A2	20060614	EP 2004-816874	20040915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.:
US 2003-504528P P 20030917
US 2004-552673P P 20040311
WO 2004-US30190 W 20040915

OTHER SOURCE(S): MARPAT 142:447211
GI



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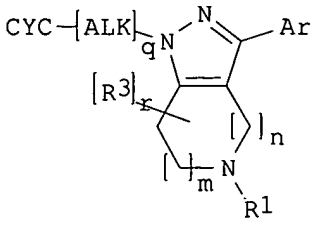

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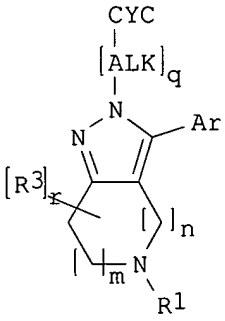
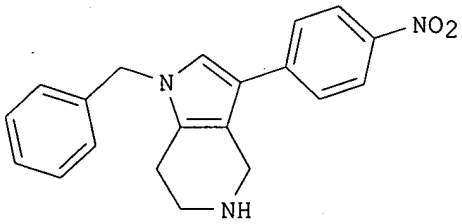


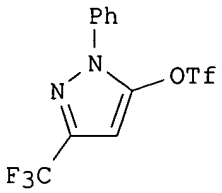
III



IV

AB The title compds. I-III [m = 0-2; n = 1-3; p = 1-3 (with the proviso that where m = 1, p is not 1); m+n ≤ 4; m+p ≤ 4; q = 0-1; r = 0-5; R3 = alkyl, allyl, propargyl, benzyl (each optionally substituted); Ar = (un)substituted (hetero)aryl; CYC = H, (un)substituted carbocyclic, heterocyclic, (hetero)aryl; R1 = H, alkyl, alkenyl, etc.; R2 = H, alkyl, alkenyl, etc.; and their pharmaceutically acceptable salts] which are serotonin modulators useful in the treatment of serotonin-mediated diseases, were prepared Thus, reacting tert-Bu 4-oxopiperidine-1-carboxylate with benzylamine in PhMe followed by addition of silica gel, and 8 h later 1-nitro-4-(2-nitrovinyl)benzene, and subsequently, after cyclization is completed, deprotection of the resulting intermediate afforded IV which showed Ki of 120 nM against 5-HT7 receptor binding.

L15 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:316491 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 143:7646
TITLE: Palladium-catalyzed coupling of pyrazole triflates with arylboronic acids
AUTHOR(S): ***Dvorak, Curt A.***; Rudolph, Dale A.; Ma, Sandy; ***Carruthers, Nicholas I.***
CORPORATE SOURCE: Johnson & Johnson Pharmaceutical Research Development, L.L.C., San Diego, CA, 92121, USA
SOURCE: Journal of Organic Chemistry (2005), 70(10), 4188-4190
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:7646
GI



I

AB A general protocol for the palladium-mediated Suzuki coupling reaction of pyrazole triflates, e.g., I, and arylboronic acids has been developed. The use of addnl. dppf ligand was determined to increase product yields allowing for the use of a broad range of reaction substrates.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

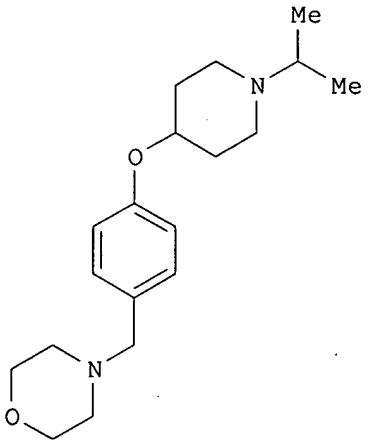
L15 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:199492 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 142:423039
TITLE: Discovery and SAR studies of a novel series of noncovalent cathepsin S inhibitors
AUTHOR(S): Gustin, Darin J.; Sehon, Clark A.; Wei, Jianmei; ***Cai, Hui***; Meduna, Steven P.; Khatuya, Haripada; Sun, Siquan; Gu, Yin; Jiang, Wen; Thurmond, Robin L.; Karlsson, Lars; ***Edwards, James P.***
CORPORATE SOURCE: Johnson and Johnson Pharmaceutical Research and Development, LLC, San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(6), 1687-1691
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:423039
AB A novel series of competitive, reversible cathepsin S (CatS) inhibitors was discovered and optimized. The 4-(2-keto-1-benzimidazolinyl)-piperidin-1-yl moiety was an effective replacement for the 4-arylpiperazin-1-yl group found in our earlier series of CatS inhibitors. This replacement imparted improved PK properties as well as decreased off-target activity. Optimization of the ketobenzimidazole moiety led to the discovery of the lead compound JNJ 10329670, which represents a novel class of selective, noncovalent, reversible, and orally bioavailable inhibitors of cathepsin S.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:191387 HCAPLUS <<LOGINID::20060731>>
TITLE: Preparation of benzimidazole carboxamides as potent human histamine H4 antagonists
AUTHOR(S): Venable, Jennifer D.; Pio, Barb; ***Dvorak, Curt A.***; Grice, Cheryl A.; Ly, Kiev S.; Shah, Chandravadan R.; Wei, Jianmei; Desai, Pragnya J.; Jiang, Wen; Nguyen, Steven; Wilson, Sandy J.; Dunford, Paul J.; Thurmond, Robin L.; Lovenberg, Timothy W.; Karlsson, Lars; ***Carruthers, Nicholas I.***; ***Edwards, James P.***

CORPORATE SOURCE: Johnson and Johnson Pharmaceutical Research and Development, LLC, San Diego, CA, 92121, USA
SOURCE: Abstracts of Papers, 229th ACS National Meeting, San Diego, CA, United States, March 13-17, 2005 (2005), MEDI-053. American Chemical Society: Washington, D. C.
CODEN: 69GQMP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB The human histamine H4 receptor was recently discovered and cloned by several groups. The expression profile includes eosinophils, mast cells, dendritic cells, and other leukocytes, implicating H4 in inflammation and regulation of the immune system. A significant medicinal chemical effort has been undertaken to discover and develop potent antagonists of the histamine H4 receptor. During the course of this effort, the synthesis of benzimidazole-2-carboxamides via benzimidazole-2-carboxylic esters was examined A single literature disclosure reported that condensation of a phenylenediamine with alkyl trialkoxyacetate forms the desired benzimidazole carboxylic ester. In our hands, treatment of phenylenediamines with Me trimethoxyacetate did not yield the desired product. However, addition of a Lewis acid catalyst, such as Yb(OTf)3, unexpectedly led to the formation of 3-methoxy-quinoxalin-2-ones in good yields. Ultimately, a general, two-step route was developed in order to obtain the desired carboxamides via variously substituted 2,2,2-trichloromethylbenzimidazoles. The synthesis and structure activity relationships (SAR), of the benzimidazole carboxamides will be discussed.

L15 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:100498 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 142:336224
TITLE: 4-Phenoxypiperidines: potent, conformationally restricted, non-imidazole histamine H3 antagonists
AUTHOR(S): ***Dvorak, Curt A.***; Apodaca, Richard; Barbier, Ann J.; Berridge, Craig W.; Wilson, Sandy J.; Boggs, Jamin D.; Xiao, Wei; Lovenberg, Timothy W.; ***Carruthers, Nicholas I.***
CORPORATE SOURCE: Johnson & Johnson Pharmaceutical Research and Development, L.L.C., San Diego, CA, 92121, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(6), 2229-2238
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:336224
GI



I

AB Two series of 4-(1-alkyl-piperidin-4-yloxy)benzonitriles and 4-(1-isopropyl-piperidin-4-yloxy)benzylamines, e.g., I, have been prepared In vitro activity was determined at the recombinant human H3 receptor and several members of these series were found to be potent H3 antagonists. The present compds. contain a 4-phenoxypiperidine core, which behaved as a conformationally restricted version of the 3-amino-1-propanol moiety common to the many previously described non-imidazole histamine H3 ligands. One selected member of the series, 4-[4-(1-isopropyl-piperidin-4-yloxy)-benzyl]-morpholine (I), was found to be a potent, highly selective H3 receptor antagonist with in vivo efficacy in a rat EEG model of wakefulness at doses as low as 1 mg/kg s.c.

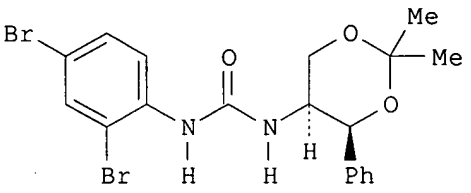
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:678931 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 141:325159
TITLE: Nonpeptidic, Noncovalent Inhibitors of the Cysteine Protease Cathepsin S
AUTHOR(S): Thurmond, Robin L.; Beavers, Mary Pat; ***Cai, Hui***; Meduna, Steven P.; Gustin, Darin L.; Sun, Siquan; Almond, Harold J.; Karlsson, Lars; ***Edwards, James P.***
CORPORATE SOURCE: Johnson Johnson Pharmaceutical Research and Development L.L.C., San Diego, CA, 92121, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(20), 4799-4801
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:325159

AB The first nonpeptidic, noncovalent inhibitors of the cysteine protease cathepsin S (CatS) are described. Electronic database searching using the program DOCK generated a screening set of potential CatS inhibitors from which two lead structures were identified as promising starting points for a drug discovery effort. Lead optimization afforded potent (IC50 < 50 nM) and selective inhibitors of CatS demonstrating cellular activity and reversibility of enzyme inhibition.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:581036 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 141:260653
TITLE: Novel substituted 4-phenyl-[1,3]dioxanes: potent and selective orexin receptor 2 (OX2R) antagonists
AUTHOR(S): McAtee, Laura C.; Sutton, Steven W.; Rudolph, Dale A.; Li, Xiaobing; Aluisio, Leah E.; Phuong, Victor K.; ***Dvorak, Curt A.***; Lovenberg, Timothy W.; ***Carruthers, Nicholas I.***; Jones, Todd K.
CORPORATE SOURCE: LLC, Johnson and Johnson Pharmaceutical Research and Development, San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(16), 4225-4229
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:260653
GI



I

AB Orexins, also termed hypocretins, consist of two neuropeptide agonists (orexin A and B) interacting with two known G-protein coupled receptors (OX1R and OX2R). In addition to other biol. functions, the orexin-2 receptor is thought to be an important modulator of sleep and wakefulness. Herein we describe a series of novel, selective OX2R antagonists consisting of substituted 4-phenyl-[1,3]dioxanes. One such antagonist is 1-(2,4-dibromo-phenyl)-3-((4S,5S)-2,2-dimethyl-4-phenyl-[1,3]dioxan-5-yl)-urea (I), which is bound by the OX2R with a pKi of 8.3, has a pKb of 7.9, and is 600-fold selective for the OX2R over the OX1R.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:220205 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 140:270852
TITLE: Preparation of nitrogen containing heterocyclic compounds as compounds useful for in the treatment of histamine H4 receptor mediated diseases
INVENTOR(S): ***Carruthers, Nicholas I.***; ***Dvorak, Curt A.***; ***Edwards, James P.***; Grice, Cheryl A.; Jablonowski, Jill A.; Ly, Kiev S.; Pio, Barbara A.; Shah, Chandravadan R.; Venable, Jennifer D.
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004022060	A2	20040318	WO 2003-US27461		20030904
WO 2004022060	C1	20040603			
WO 2004022060	A3	20040708			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2497827	AA	20040318	CA 2003-2497827		20030904
US 2004058934	A1	20040325	US 2003-655381		20030904
AU 2003265886	A1	20040329	AU 2003-265886		20030904
EP 1545532	A2	20050629	EP 2003-794573		20030904
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BR 2003014059	A	20050705	BR 2003-14059		20030904
CN 1694704	A	20051109	CN 2003-824969		20030904
JP 2006500390	T2	20060105	JP 2004-534443		20030904
US 2004127395	A1	20040701	US 2003-656385		20030905
NO 2005001694	A	20050405	NO 2005-1694		20050405
PRIORITY APPLN. INFO.:			US 2002-408569P	P	20020906
			US 2002-408579P	P	20020906
			US 2002-408736P	P	20020906
			WO 2003-US27461	W	20030904

OTHER SOURCE(S): MARPAT 140:270852
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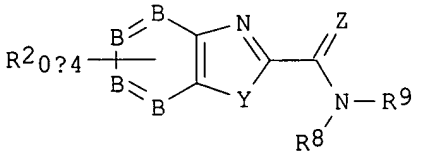

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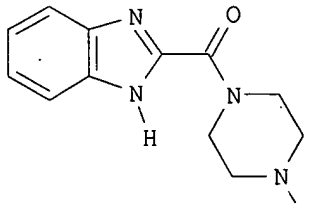


II

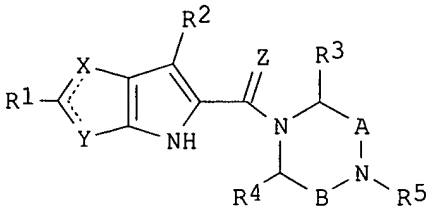
AB Title compds. I [B = C or up to one N; Y = O, S, NH, or alkyl substituted N; Z = O or S; R2 independently = H, halo, alkyl, alkoxy, cycloalkyl, etc.; R8 = H and R9 = (un)substituted azabicyclo[3.2.1]oct-3-yl moiety; or R8 and R9 together form an (un)substituted dinitrogen heterocycle] are prepared and disclosed as histamine H4 receptor antagonists. Thus, e.g., II

was prepared by reaction of phenylenediamine with Me 2,2,2-trichloroacetimidate to provide intermediate 2-trichloromethyl-1H-benzoimidazole which was treated with N-methylpiperazine followed by K2CO3. In binding assays to human histamine H4 receptor, I possessed Ki values of 11-8000 nM. I are useful to treat or prevent disorders and conditions mediated by the histamine H4 receptor, including allergic rhinitis.

L15 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:203556 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 140:235696
TITLE: Preparation of piperazinecarbonyl heterocyclic compounds as histamine H4 antagonists
INVENTOR(S): ***Cai, Hui; Carruthers, Nicholas I.; Dvorak, Curt A.; Edwards, James P.; Kwok, Annette K.***
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004048878	A1	20040311	US 2003-656059		20030905
CA 2497868	AA	20040318	CA 2003-2497868		20030905
WO 2004022537	A2	20040318	WO 2003-US28017		20030905
WO 2004022537	A3	20040506			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003272285	A1	20040329	AU 2003-272285		20030905
EP 1543011	A2	20050622	EP 2003-754461		20030905
EP 1543011	B1	20060503			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2006500394	T2	20060105	JP 2004-534722		20030905
PRIORITY APPLN. INFO.:			US 2002-408723P	P	20020906
			WO 2003-US28017	W	20030905

OTHER SOURCE(S): MARPAT 140:235696
GI



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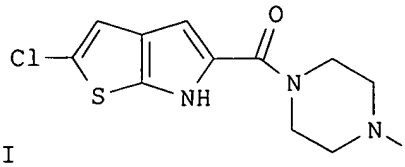


II

AB Thienopyrrolyl and furanopyrrolyl compds. of formula I [X, Y = CR6, O, S; Z = O, S; R1, R6 = H, halo, alkyl, alkoxy, etc.; R2 = H, halo, alkyl; R3, R4 = H, alkyl, cycloalkyl, etc.; R5 = H, CN, alkyl, etc.; A = (substituted) (CH2)m; B = (substituted) (CH2)n; m, n = 1-2; AR5 = alkylene, heteroalkylene] are prepared which are useful to treat or prevent disorders and conditions mediated by the histamine H4 receptor, including allergic rhinitis. Thus, II was prepared by annulation of thiophene-3-carboxaldehyde and Et azidoacetate, hydrolysis, reaction with N-chlorosuccinimide, then amidation with N-methylpiperazine. The Ki value of II was 25 nM against human histamine H4 receptor.

L15 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:65340 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 140:264061
TITLE: Identification of a potent and selective noncovalent cathepsin S inhibitor
AUTHOR(S): Thurmond, Robin L.; Sun, Siquan; Sehon, Clark A.; Baker, Sherry M.; ***Cai, Hui***; Gu, Yin; Jiang, Wen; Riley, Jason P.; Williams, Kacy N.; ***Edwards, James P.***; Karlsson, Lars
CORPORATE SOURCE: Johnson and Johnson Pharmaceutical Research and Development, L.L.C., San Diego, CA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 308(1), 268-276
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cathepsin S is considered crucial for normal presentation of major histocompatibility complex (MHC) class II-restricted antigens by antigen presenting cells to CD4+ T cells. It is a key enzyme for the degradation of the class II-associated invariant chain, a process that is required for effective antigen loading of class II mols. Here, we report a selective, orally available, high-affinity cathepsin S inhibitor, 1-[3-[4-(6-Chloro-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]propyl]-4,5,6,7-tetrahydro-5-(methylsulfonyl)-3-[4-(trifluoromethyl)phenyl]-1H-pyrazolo[4,3-c]pyridine, (JNJ 10329670), that represents a novel class of immunosuppressive compds. JNJ 10329670 is a highly potent (Ki of .apprx.30 nM), nonpeptidic, noncovalent inhibitor of human cathepsin S, but it is much less active against the mouse, dog, monkey, and bovine enzymes. The compound is inactive against other proteases, including the closely related cathepsins L, F, and K. This selectivity makes JNJ 10329670 an excellent tool for exploring the role of cathepsin S in human systems. Treatment of human B cell lines and primary human dendritic cells with JNJ 10329670 resulted in the accumulation of the p10 fragment of the invariant chain (IC50 of .apprx.1 μM). In

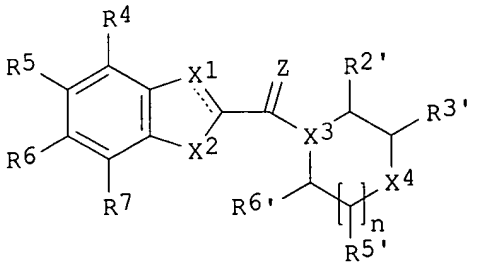
contrast, inhibition of invariant chain proteolysis was much less effective in a human monocytic cell line, suggesting that other enzymes may degrade the invariant chain in this cell type. JNJ 10329670 was shown to block the proteolysis of the invariant chain in vivo by using immunocompromised mice injected with human peripheral blood mononuclear cells (PBMCs). Furthermore, this inhibitor blocks the presentation of tetanus toxoid and giant ragweed by human PBMCs. The properties of JNJ 10329670 make it a candidate for immunosuppressive therapy of allergies and autoimmune diseases.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:874968 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 139:364959
TITLE: Preparation of heterocyclic compounds for treatment of H4-mediated conditions
INVENTOR(S): ***Carruthers, Nicholas I.***; Chai, Wenying; ***Dvorak, Curt A.***; ***Edwards, James P.***; Grice, Cheryl A.; Jablonowski, Jill A.; Karlsson, Lars; Khatuya, Haripada; Kreisberg, Jennifer D.; ***Kwok, Annette K.***; Lovenberg, Timothy W.; Ly, Kiev S.; Pio, Barbara; Shah, Chandravadan R.; Sun, Siquan; Thurmond, Robin L.; Wei, Jianmei; Xiao, Wei
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 43 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003207893	A1	20031106	US 2002-94357		20020308
US 6803362	B2	20041012			
US 2005085487	A1	20050421	US 2004-961247		20041008
PRIORITY APPLN. INFO.:			US 2001-274900P	P	20010309
			US 2001-343259P	P	20011221
			US 2002-94357	A3	20020308

OTHER SOURCE(S): MARPAT 139:364959
GI



I

AB Heterocyclic compds. [I; R1 = Ra, RaRb-, RaORb-, or (Rc)(Rd)N-Rb-; where

Ra = H, cyano, (CO)N(Rc)(Rd), C(:NH)(NH2), C1-10 alkyl, C3-8 alkenyl, C3-8 cycloalkyl, C2-5 heterocyclic radical, Ph; Rb = C1-8 alkylene, C2-8 alkenylene, C3-8 cycloalkylene, bivalent C3-8 heterocyclic radical, or phenylene; Rc, Rd = independently H, C1-8 alkyl, C2-8 alkenyl, C3-8 cycloalkyl, Ph; R2', R3' = H, Me, Et, NRpRq, -CONRpRq, -CO2Rr, -CH2NRpRq, or CH2ORr; Rp, Rq, Rr = C1-6 alkyl, C3-6 cycloalkyl, Ph, (C3-6 cycloalkyl)(C1-2 alkylene), benzyl, phenethyl; or NpRq together form s 5-7 membered heterocyclic ring; R5', R6' = H, Me, Et; X4 = (un)substituted NH or S; X1 = CR3; R3 = F, Cl, Br, CHO, Rf, RfRg-, Rf-O-Rg-, (Rh)(Ri)NRg-; where Rf = H, C1-6 alkyl, C2-6 alkenyl, C3-6 cycloalkyl, Ph, etc.; Rg = C1-6 alkylene, C2-6 alkenylene, C3-6 cycloalkylene, bivalent C3-6 heterocyclic radical, or phenylene; Rh, Ri = each independently H, C1-6 alkyl, C2-6 alkenyl, C3-6 cycloalkyl, or phenyl; X2 = (un)substituted NH, O, provided that X2 is (un)substituted NH where X1 is N; Re = H, C1-6 alkyl; X3 = N; Z = O, S; R4, R6 = H, F, Cl, Br, iodo, CO2H, OH, NO2, cyano, C1-4 alkoxy, etc.; R5, R7 = H, F, Cl, Br, iodo, OH, nitro, (un)substituted NH2, cyano, Ph, OCH2Ph, C1-4 alkoxy, etc.; wherein n is 0, 1, or 2] or pharmaceutically acceptable salts, esters, or amides thereof are prepared These compds. are histamine H4 receptor antagonists and useful for the treatment of histamine H4-mediated conditions including inflammatory disorders, asthma, psoriasis, rheumatoid arthritis, ulcerative colitis, Crohn's disease, inflammatory bowel disease, multiple sclerosis, allergic disorders, autoimmune disease, lymphatic disorders, and immunodeficiency disorders. The inflammatory disorders include acute inflammation, allergic inflammation, and chronic inflammation. For example, (5-Chloro-1H-indol-2-yl)(4-methylpiperazin-1-yl)methanone at 10 mg/kg blocked 62% the peritonitis induced by zymosan.

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:865554 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 140:93879
TITLE: A practical parallel synthesis of 2-substituted indolizines
AUTHOR(S): Chai, Wenying; ***Kwok, Annette***; Wong, Victoria; ***Carruthers, Nicholas I.***; Wu, Jiejun
CORPORATE SOURCE: Johnson and Johnson Pharmaceutical Research and Development L.L.C, San Diego, CA, 92121, USA
SOURCE: Synlett (2003), (13), 2086-2088
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:93879

AB A practical parallel synthesis of 2-substituted indolizines via Chichibabin reactions of picolines with α-bromo ketones is reported. The phase-separation techniques was used for the product purification Further transformation of indolizines obtained into the corresponding indolizidines by catalytic hydrogenation is also described.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:634919 HCAPLUS <<LOGINID::20060731>>
TITLE: Discovery of the first potent and selective non-imidazole human histamine H4 receptor antagonists
AUTHOR(S): Jablonowski, Jill A.; Grice, Cheryl A.; Chai, Wenying;

Dvorak, Curt A.; Kreisberg, Jennifer D.; ***Kwok, Annette K.***; Ly, Kiev S.; Wei, Jianmei; Baker, Sherry M.; Desai, Pragyna J.; Jiang, Wen; Wilson, Sandy J.; Thurmond, Robin L.; Karlsson, Lars; ***Edwards, James P.***; Lovenberg, Timothy W.; ***Carruthers, Nicholas I.***

CORPORATE SOURCE: Neuroscience, Johnson & Johnson Pharmaceutical Research and Development, LLC, San Diego, CA, 92121, USA

SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-311. American Chemical Society: Washington, D. C.
CODEN: 69EKY9

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Following the discovery of the human histamine H4 receptor, we set out to identify potent, selective, non-imidazole histamine H4 ligands. We began with a high throughput screen of our corporate compound collection, which produced several lead compds. including indolylpiperazines. Based on these leads, a medicinal chemical program was initiated to evaluate the structure activity relationships (SAR) for the indolylpiperazines 1. The SAR for this series and the biol. evaluation of selected analogs will be discussed.

L15 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:634664 HCAPLUS <<LOGINID::20060731>>

TITLE: Diamine-based human histamine H3 receptor antagonists

AUTHOR(S): Apodaca, Richard; ***Dvorak, Curt A.***; Xiao, Wei; Barbier, Ann J.; Boggs, Jamin D.; Wilson, Sandy J.; Lovenberg, Timothy W.; ***Carruthers, Nicholas I.***

CORPORATE SOURCE: Neuroscience, Johnson & Johnson Pharmaceutical Research and Development, LLC, San Diego, CA, 92121, USA

SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-055. American Chemical Society: Washington, D. C.
CODEN: 69EKY9

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB The histamine H3 receptor mediates the release of histamine and other neurotransmitters in the CNS, in addition to other functions. Structure-activity relationships available to us through high throughput screening of our corporate compound collection against the human H3 receptor, and some published work available at the time, suggested a remarkably simple pharmacophore consisting of two basic nitrogen atoms flanking a lipophilic core. We reasoned that a readily-accessed chemical series that incorporated this structural motif could furnish a viable platform for the development of H3 receptor ligands with drug-like properties. To test this idea, a series of 4-(aminoalkoxy)benzylamines was selected. The synthesis and in vitro biol. properties of these and related compds. will be discussed.

L15 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:563314 HCAPLUS <<LOGINID::20060731>>

DOCUMENT NUMBER: 139:239681

TITLE: The First Potent and Selective Non-Imidazole Human

Histamine H4 Receptor Antagonists
AUTHOR(S): Jablonowski, Jill A.; Grice, Cheryl A.; Chai, Wenying; ***Dvorak, Curt A.***; Venable, Jennifer D.; ***Kwok, Annette K.***; Ly, Kiev S.; Wei, Jianmei; Baker, Sherry M.; Desai, Pragyna J.; Jiang, Wen; Wilson, Sandy J.; Thurmond, Robin L.; Karlsson, Lars; ***Edwards, James P.***; Lovenberg, Timothy W.; ***Carruthers, Nicholas I.***
CORPORATE SOURCE: Johnson & Johnson Pharmaceutical Research and Development, L.L.C, San Diego, CA, 92121, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(19), 3957-3960
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:239681
AB Following the discovery of the human histamine H4 receptor, a high throughput screen of our corporate compound collection identified a potential lead compound Investigation of the structure-activity relationship (SAR) resulted in the discovery of novel compds., which are the first potent and selective histamine H4 receptor antagonists to be described.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:560207 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 139:245874
TITLE: A New Class of Diamine-Based Human Histamine H3 Receptor Antagonists: 4-(Aminoalkoxy)benzylamines
AUTHOR(S): Apodaca, Richard; ***Dvorak, Curt A.***; Xiao, Wei; Barbier, Ann J.; Boggs, Jamin D.; Wilson, Sandy J.; Lovenberg, Timothy W.; ***Carruthers, Nicholas I.***
CORPORATE SOURCE: Johnson & Johnson Pharmaceutical Research & Development, L.L.C., San Diego, CA, 92121, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(18), 3938-3944
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:245874
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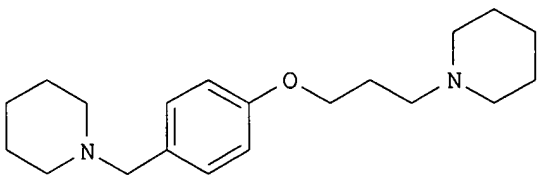


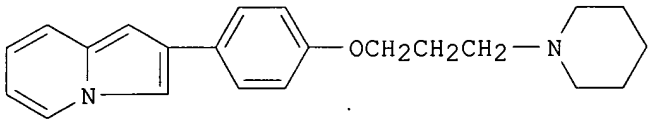
I

AB (substituted aminoalkoxybenzyl)piperidines such as I are prepared as potential selective human histamine H3 receptor antagonists. Replacement

of either the piperidine nitrogen of (substituted aminoalkoxybenzyl)piperidines or the nitrogen of the aminoalkoxybenzyl moiety with a methine group yields analogs with significantly reduced binding affinities for the histamine H3 receptor. Some (aminoalkoxybenzyl)piperidines exhibit subnanomolar binding affinities for the human histamine H3 receptor. For example, I has a pKi value of 9.24 at the human histamine H3 receptor with selectivity of >1000 for the H3 receptor subtype over the histamine H1, H2, and H4 receptor subtypes; I is also highly selective for the histamine H3 receptor over a variety of other receptors and ion channels. I is found to possess good permeability and liver microsomal stability with moderate binding to human plasma proteins.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:326033 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 139:230551
TITLE: Non-imidazole heterocyclic histamine H3 receptor antagonists
AUTHOR(S): Chai, Wenying; Breitenbucher, J. Guy; ***Kwok, Annette***; Li, Xiaobing; Wong, Victoria; ***Carruthers, Nicholas I.***; Lovenberg, Timothy W.; Mazur, Curt; Wilson, Sandy J.; Axe, Frank U.; Jones, Todd K.
CORPORATE SOURCE: Johnson & Johnson Pharmaceutical Research and Development L. L. C., San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(10), 1767-1770
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:230551
GI



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AB Continued exploration of the SAR around the lead imidazopyridine histamine H3 antagonist has led to the discovery of several related series of heterocyclic histamine H3 antagonists. The synthesis and SAR of indolizine, indole, and pyrazolopyridine based compds. are now described. E.g., indolizine I was prepared and its histamine H3 antagonist activity determined

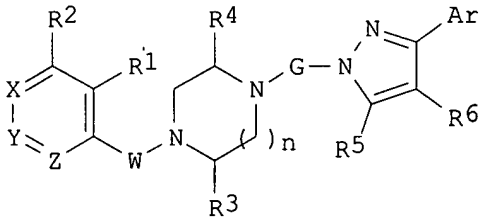
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:300610 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 138:304307
TITLE: Preparation of piperazinylpropylpyrazolopyridines for treatment of allergy

INVENTOR(S): Breitenbucher, J. Guy; ***Cai, Hui***; ***Edwards, James P.***; Grice, Cheryl A.; Gu, Yin; Gustin, Darin J.; Karlsson, Lars; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Sun, Siquan; Tays, Kevin L.; Thumond, Robin L.; Wei, Jianmei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 47 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073672	A1	20030417	US 2001-947041	20010905
PRIORITY APPLN. INFO.:			US 2001-947041	20010905

OTHER SOURCE(S): MARPAT 138:304307
GI



I

AB Use of title compds. [I; R1 = H, N3, halo, alkoxy, OH, alkyl, alkenyl, cyano, NO2, amino, acyl, etc.; R2 = H, halo, alkoxy, alkyl, alkenyl, haloalkyl, cyano, amino; R1R2, R5R6 = atoms to form a (substituted) (unsatd.) 5-7 membered (hetero)cycle; R3, R4 = H, alkyl; R5, R6 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, 4-7 membered carbocyclyl, heterocyclyl; Ar = (substituted) mono- or bicyclic aryl, heteroaryl; W = SO2, CO, bond, CHR20; R20 = H, alkyl, Ph, PhCH2, naphthyl, heterocyclyl; X = N, R12C; Y = N, R13C; Z = N, R14C; R12-R14 = H, halo, alkoxy, alkyl, alkenyl, cyano, NO2, amino, acyl, haloalkyl, heterocyclyl, heterocyclylalkyl, sulfonylamino, etc.; WR1 = atoms to form rings; G = (substituted) alkylene; n = 1,2], for treatment of allergy is claimed. Thus, 1-[3-(4-chlorophenyl)-1-(3-chloropropyl)-1,4,6,7-tetrahydropyrazolo[4.3-c]pyridin-5-yl]ethanone (preparation given), 1-(2-fluorophenyl)piperazine, K2CO3, and Bu4NI were stirred in MeCN for 7 days to give 41% 1-[3-(4-chlorophenyl)-1-[3-[4-(2-fluorophenyl)piperazin-1-yl]propyl]-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone. The latter inhibited human cathepsin S with IC50 = 0.89 μM.

L15 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:282117 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 138:304277
TITLE: Preparation of 3-phenyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines as cathepsin S inhibitors for treating allergies
INVENTOR(S): Breitenbucher, J. Guy; ***Cai, Hui***; ***Edwards, James P.***; Grice, Cheryl A.; Gu, Yin;

Gustin, Darin J.; Karlsson, Lars; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Sun, Siquan; Tays, Kevin L.; Thurmond, Robin L.; Wei, Jianmei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 928,122.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003069240	A1	20030410	US 2002-75673		20020213
US 2002040020	A1	20020404	US 2001-928122		20010810
PRIORITY APPLN. INFO.:			US 2001-928122	A2	20010810
			US 2000-225138P	P	20000814

OTHER SOURCE(S): MARPAT 138:304277
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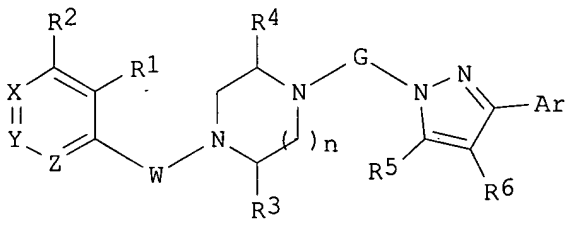

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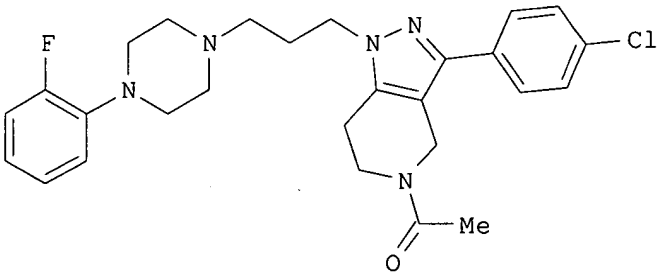


II

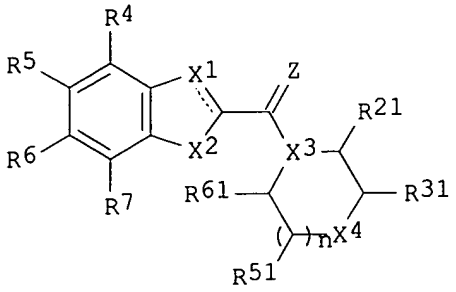
AB Title compds. I [wherein Ar = (un)substituted mono- or bicyclic (hetero)aryl; G = (un)substituted alkenediyl or alkanediyl; W = SO2, CO, (un)substituted C, or a bond; or W and R1 taken together with the 6 membered ring to which they are attached form benzimidazolyl, benzothiazolyl, benz(is)oxazolyl, etc.; X, Y, and Z = independently N or (un)substituted C; R1 = H, N3, halo, alkoxy, OH, alkyl, alkenyl, CN, NO2, acyl, or (un)substituted amino, carboxy, carbamoyl, or sulfamoyl; R2 = H, halo, alkoxy, (halo)alkyl, alkenyl, CN, or (un)substituted amino; or R1R2 = (un)substituted carbocyclic or heterocyclic ring; R3 and R4 = independently H or alkyl; R5 and R6 = independently H, alkyl, alkenyl, alkoxy, alkylthio, halo, carbocyclyl, or heterocyclyl; or R5R6 = (un)substituted carbocyclic or heterocyclic ring; n = 1-2; or

pharmaceutically acceptable salts, amides, or esters thereof] were prepared as cathepsin S inhibitors for the treatment of an allergic condition, including an atopic allergic conditions. For example, N-acetyl-4-piperidone was condensed with morpholine in the presence of TsOH to give the enamine. Reaction with 4-ClC6H4COCl , followed by cycloaddn. with H2NNH2, gave 1-[3-(4-chlorophenyl)-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone (42%). Alkylation with 1-bromo-3-chloropropane (83%) and addition of 1-(2-fluorophenyl)piperazine afforded II (41%). The latter inhibited recombinant human cathepsin S with IC50 of 0.89 μM.

L15 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:716248 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 137:232678
TITLE: Preparation of piperazinylcarbonylindoles as histamine H4 antagonists.
INVENTOR(S): ***Carruthers, Nicholas I.***; Chai, Wenying; ***Dvorak, Curt A.***; ***Edwards, James P.***; Grice, Cheryl A.; Jablonowski, Jill A.; Karlsson, Lars; Khatuya, Haripada; Kreisberg, Jennifer D.; ***Kwok, Annette K.***; Lovenberg, Timothy W.; Ly, Kiev S.; Pio, Barbara; Shah, Chandravadan R.; Sun, Siquan; Thurmond, Robin L.; Wei, Jianmei; Xiao, Wei
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002072548	A2	20020919	WO 2002-US7168		20020308
WO 2002072548	A3	20021212			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2440438	AA	20020919	CA 2002-2440438		20020308
AU 2002336273	A1	20020924	AU 2002-336273		20020308
EP 1373204	A2	20040102	EP 2002-750590		20020308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004520434	T2	20040708	JP 2002-571464		20020308
PRIORITY APPLN. INFO.:			US 2001-274900P	P	20010309
			US 2001-343259P	P	20011221
			WO 2002-US7168	W	20020308

OTHER SOURCE(S): MARPAT 137:232678
GI



I

AB Title compds. [I; R1 = Ra, RaRb, RaORb, RcRdNRb; Ra = H, cyano, CONRcRd, C(:NH)(NH2), alkyl, alkenyl, cycloalkyl, heterocyclyl, Ph; Rb = alkylene, alkenylene, cycloalkylene, heterocyclylene, phenylene; Rc, Rd = H, alkyl, alkenyl, cycloalkyl, Ph; R21 = H, Me, Et, NRpRq, CONRpRq, CO2Rr, CH2NRpRq, CH2ORr; Rp, Rq, Rr = alkyl, cycloalkyl, Ph, cycloalkylalkylene, PhCH2, phenethyl; RpRqN = 4-7 membered heterocyclyl; R31 = H, Me, Et, NRsRt, CONRsRt, CO2Ru, CH2NRsRt, CH2ORu; Rs, Rt, Ru = alkyl, cycloalkyl, Ph, cycloalkylalkylene, PhCH2, phenethyl; RsRtN = heterocyclyl; R51, R61, R71 = Me, Et, H; X4 = NR1, S; X1 = CR3; R3 = F, Cl, Br, CHO, Rf, RfRg, RrORg, RhRjNRg; Rf = H, alkyl, alkenyl, cycloalkyl, heterocyclyl, Ph; Rg = alkylene, alkenylene, cycloalkylene, heterocyclylene, phenylene; Rh Ri, = H, alkyl, alkenyl, cycloalkyl, Ph; X2 = NRe, O; Re = H, alkyl; X3 = N; Z = O, S; R4, R6 = H, F, Cl, Br, iodo, CO2H, OH, NO2, amino, cyano, alkoxy, alkyl; R5 = H, F, Cl, Br, iodo, CORj, OH, NO2, NRjRk, cyano, Ph, OCH2Ph, alkoxy, alkyl; R7 = H, F, Cl, Br, iodo, CORm, OH, NO2, cyano, Ph, alkyl, etc.; Rj, Rk, Rl, Rm = H, alkyl, OH, Ph, PhCH2, phenethyl, alkoxy; n = 0, 1, 2; with provisos], were prepared Thus, 5-chloroindole-2-carboxylic acid, HATU, HOAT, diisopropylethylamine, N-methylpiperazine were stirred 48 h in DMF to give (5-chloro-1H-indol-2-yl)(4-methylpiperazin-1-yl)methanone. The latter showed Ki = 0.005 μM in an H4 binding assay.

L15 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:520410 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 137:242380
TITLE: Reconsideration of 5-hydroxytryptamine (5-HT)7 receptor distribution using [3H]5-carboxamidotryptamine and [3H]8-hydroxy-2-(di-n-propylamino)tetraline: analysis in brain of 5-HT1A knockout and 5-HT1A/1B double-knockout mice
AUTHOR(S): Bonaventure, Pascal; Nepomuceno, Diane; ***Kwok, Annette***; Chai, Wenying; Langlois, Xavier; Hen, Rene; Stark, Kimberly; ***Carruthers, Nicholas***; Lovenberg, Timothy W.
CORPORATE SOURCE: Johnson and Johnson Pharmaceutical Research and Development L.L.C, San Diego, CA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 302(1), 240-248
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The characterization and anatomical distribution of 5-hydroxytryptamine (5-HT)7 receptor binding sites in brain tissue has been hampered by the lack of a specific radioligand. In the present autoradiog. study, we took

advantage of 5-HT1A knockout and 5-HT1A/1B double-knockout mice to revisit the pharmacol. characterization and anatomical localization of 5-HT7 binding sites in mouse brain using [3H]5-carboxamidotryptamine (5-CT) and [3H]8-hydroxy-2-(di-n-propylamino)tetraline (8-OH-DPAT). The distribution pattern of [3H]5-CT binding sites (2 nM) in the brain of mice lacking the 5-HT1A/1B receptor was scarce and confined to the septum, globus pallidus, thalamus, hypothalamus, amygdala, cortex, and substantia nigra. The low densities of [3H]5-CT binding sites detected in septum, thalamus, hypothalamus, amygdala, and cortex were displaced by 10 μM of the selective 5-HT7 receptor antagonist (R)-3-(2-(2-(4-methylpiperidin-1-yl)ethyl)pyrrolidine-1-sulfonyl) phenol (SB-269970). The SB-269970-insensitive [3H]5-CT binding sites detected in globus pallidus and substantia nigra of 5-HT1A/1B knockout mice were displaced by N-[3-(2-dimethylamino)ethoxy-4-methoxy-phenyl]-2'-methyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-(1,1'-biphenyl)-4-carboxamide hydrochloride (SB-216641) (1 μM), demonstrating the 5-HT1D nature of these binding sites. In contrast to the low densities of [3H]5-CT binding sites, high-to-moderate densities of [3H]8-OH-DPAT binding sites (10 nM) were found throughout the brain of 5-HT1A and 5-HT1A/1B knockout mice (olfactory system, septum, thalamus, hypothalamus, amygdala, CA3 field of the hippocampus, cortical mantle, and central gray). These [3H]8-OH-DPAT binding sites were displaced by 10 μM SB-269970, risperidone, and methiothepin but not by pindolol, N-tert-butyl-3-[4-(2-methoxyphenyl)piperazin-1-yl]-2-phenylpropanamide (WAY-100135), or citalopram. We conclude that despite its high affinity for the 5-HT7 receptor in tissue homogenates, [3H]5-CT is not a good tracer for measuring 5-HT7 receptor binding sites autoradiog. Also, the lower affinity ligand [3H]8-OH-DPAT is a much better tracer for autoradiog. studies at the 5-HT7 receptor binding sites.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:240772 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 136:263105
TITLE: Octahydroindolizine and quinolizine and hexahydropyrrolizine derivatives as histaminic H1 and H3 antagonists
INVENTOR(S): Apodaca, Richard; ***Carruthers, Nicholas I.***; Carson, John R.; Chai, Wenying; ***Kwok, Annette K.***; Li, Xiaobing; Lovenberg, Timothy W.; Rudolph, Dale A.; Shah, Chandravadan R.
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024695	A2	20020328	WO 2001-US29624	20010921
WO 2002024695	A3	20020919		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,

UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2423284	AA	20020328	CA 2001-2423284	20010921
AU 2001092936	A5	20020402	AU 2001-92936	20010921
US 2003013733	A1	20030116	US 2001-960031	20010921
EP 1326863	A2	20030716	EP 2001-973346	20010921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004510712	T2	20040408	JP 2002-529105	20010921
US 2004167336	A1	20040826	US 2004-773808	20040206
US 2005288323	A1	20051229	US 2005-205958	20050817

PRIORITY APPLN. INFO.:

US 2000-234504P	P	20000922
US 2000-234505P	P	20000922
US 2000-234604P	P	20000922
US 2001-960031	B1	20010921
WO 2001-US29624	W	20010921
US 2004-773808	A1	20040206

OTHER SOURCE(S): MARPAT 136:263105

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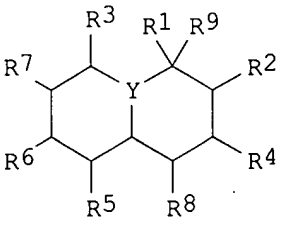

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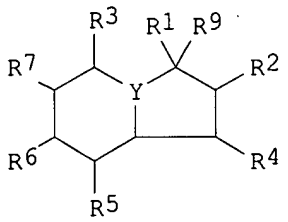

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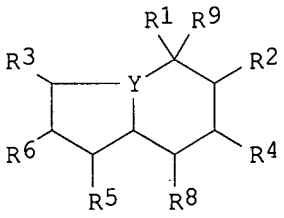
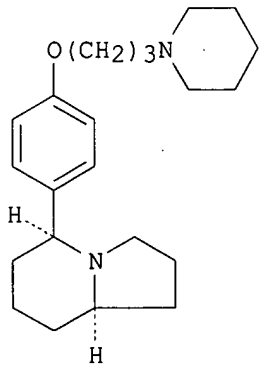


III



IV

AB Title compds. I-III [Y = N, N=O; one of R1-R3 = substituted cycloalkyl, Ph, naphthyl, heterocyclyl, cycloalkylalkyl, phenylalkyl, naphthylalkyl, heterocyclylalkyl, the others are H, halogen, alkyl; R4, R5, R7, R8 = H, halogen, alkyl, alkoxy; R6 = H, O, Ph; R9 = H, CN, alkyl, alkylamino] were prepared for use as histaminic H1 and H3 antagonists in treatment of histamine-mediated diseases and conditions. Thus, the indolizine IV was prepared by reaction of 4-H2N(CH2)3CH(OMe)2 with OC(CH2CO2Et)2 and 4-MeOC6H4CHO to give 5-(4-methoxyphenyl)-7(8H)-indolizinone, reduction of the

oxo group, demethylation, and reaction with 1-(3-chloropropyl)piperidine. IV had a Ki of 0.7 nM for N-methylhistamine binding.

L15 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:184900 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 136:247577
TITLE: Preparation of 3-phenyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines as cathepsin S inhibitors for treating allergies
INVENTOR(S): ***Cai, Hui; Edwards, James P.***; Gu, Yin; Karlsson, Lars; Meduna, Steven P.; Pio, Barbara A.; Sun, Siquan; Thurmond, Robin L.; Wei, Jianmei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020013	A2	20020314	WO 2001-US27480	20010905
WO 2002020013	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002040019	A1	20020404	US 2001-927188	20010810
US 6635633	B2	20031021		
CA 2421510	AA	20020314	CA 2001-2421510	20010905
AU 2001088731	A5	20020322	AU 2001-88731	20010905
EP 1315492	A2	20030604	EP 2001-968487	20010905
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JP 2004508330	T2	20040318	JP 2002-524497	20010905
CN 1505509	A	20040616	CN 2001-818504	20010905
NZ 524682	A	20041126	NZ 2001-524682	20010905
RU 2259202	C2	20050827	RU 2003-106190	20010905
US 2005234102	A1	20051020	US 2005-147923	20050608
PRIORITY APPLN. INFO.:			US 2000-230407P P	20000906
			US 2001-927188 A	20010810
			US 2000-225178P P	20000814
			WO 2001-US27480 W	20010905
			US 2003-401486 A1	20030328

OTHER SOURCE(S): MARPAT 136:247577
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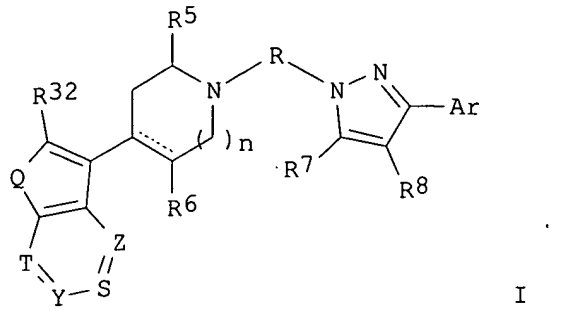

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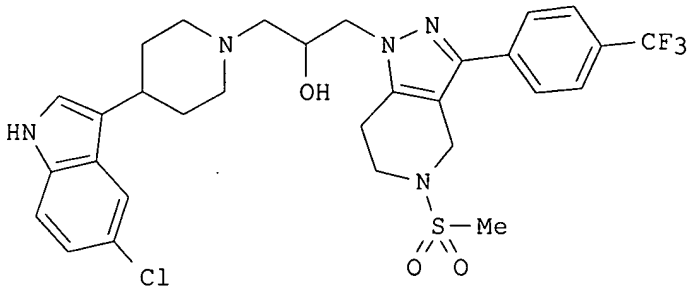

II

AB Title compds. I [wherein Ar = (un)substituted mono- or bicyclic (hetero)aryl; G = (un)substituted alkenediyl or alkanediyl; Q = O, S, or (un)substituted N; S, T, Y, and Z = independently N or (un)substituted C; R5 and R6 = independently H or alkyl; R7 and R8 = independently H, alkyl, alkenyl, alkoxy, alkylthio, halo, carbocyclyl, or heterocyclyl; or R7R8 = (un)substituted carbocyclic or heterocyclic ring; R32 = H, (hydroxy)alkyl, CN, acyl, carbamoyl, CHO, or alkoxycarbonyl; n = 0-2; or pharmaceutically acceptable salts, amides, esters, or stereoisomers thereof] were prepared as cathepsin S inhibitors for the treatment of an allergic condition, including an atopic allergic conditions. For example, 1-methanesulfonylpiperidin-4-one (preparation given) was condensed with morpholine in the presence of TsOH to give the enamine. Reaction with 4-CF3C6H4COCl, followed by cycloaddn. with H2NNH2, gave 5-methanesulfonyl-3-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydro-1H-pyrazol[4,3-c]pyridine (72%). Alkylation with epichlorohydrin (35%) and addition of 5-chloro-3-piperidin-4-yl-1H-indole (preparation given) afforded II (88%). The latter inhibited recombinant human cathepsin S with IC50 of 0.07 μM.

L15 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:184899 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 136:247576
TITLE: Preparation of 3-phenyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines as cathepsin S inhibitors for treating allergies
INVENTOR(S): Breitenbucher, J. Guy; ***Cai, Hui***; ***Edwards, James P.***; Grice, Cheryl A.; Gu, Yin; Gustin, Darin J.; Karlsson, Lars; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Sun, Siquan; Tays, Kevin L.; Thurmond, Robin L.; Wei, Jianmei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020012	A2	20020314	WO 2001-US27479	20010905
WO 2002020012	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002040020	A1	20020404	US 2001-928122	20010810
CA 2421505	AA	20020314	CA 2001-2421505	20010905
AU 2001088730	A5	20020322	AU 2001-88730	20010905
EP 1315491	A2	20030604	EP 2001-968486	20010905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004508329	T2	20040318	JP 2002-524496	20010905
NZ 524680	A	20040924	NZ 2001-524680	20010905
RU 2277909	C2	20060620	RU 2003-106191	20010905
PRIORITY APPLN. INFO.:			US 2000-230407P P	20000906
			US 2001-928122 A	20010810
			US 2000-225138P P	20000814
			WO 2001-US27479 W	20010905

OTHER SOURCE(S): MARPAT 136:247576
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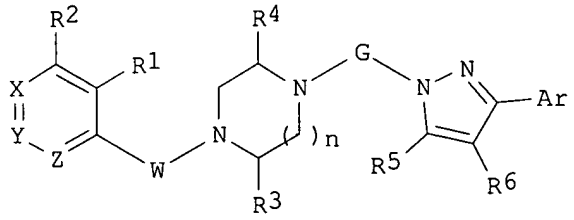

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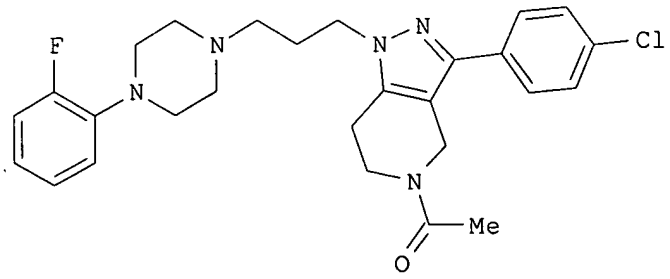


II

AB Title compds. I [wherein Ar = (un)substituted mono- or bicyclic (hetero)aryl; G = (un)substituted alkenediyl or alkanediyl; W = SO2, CO, (un)substituted C, or a bond; or W and R1 taken together with the 6 membered ring to which they are attached form benzimidazolyl, benzothiazolyl, benz(is)oxazolyl, etc.; X, Y, and Z = independently N or (un)substituted C; R1 = H, N3, halo, alkoxy, OH, alkyl, alkenyl, CN, NO2, acyl, or (un)substituted amino, carboxy, carbamoyl, or sulfamoyl; R2 = H, halo, alkoxy, (halo)alkyl, alkenyl, CN, or (un)substituted amino; or R1R2 = (un)substituted carbocyclic or heterocyclic ring; R3 and R4 = independently H or alkyl; R5 and R6 = independently H, alkyl, alkenyl, alkoxy, alkylthio, halo, carbocyclyl, or heterocyclyl; or R5R6 = (un)substituted carbocyclic or heterocyclic ring; n = 1-2; or pharmaceutically acceptable salts, amides, or esters thereof] were prepared as cathepsin S inhibitors for the treatment of an allergic condition, including an atopic allergic conditions. For example, N-acetyl-4-piperidone was condensed with morpholine in the presence of TsOH to give the enamine. Reaction with 4-ClC6H4COCl , followed by cycloaddn. with H2NNH2, gave 1-[3-(4-chlorophenyl)-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone (42%). Alkylation with 1-bromo-3-chloropropane (83%) and addition of 1-(2-fluorophenyl)piperazine afforded II (41%). The latter inhibited recombinant human cathepsin S with IC50 of 0.89 μM.

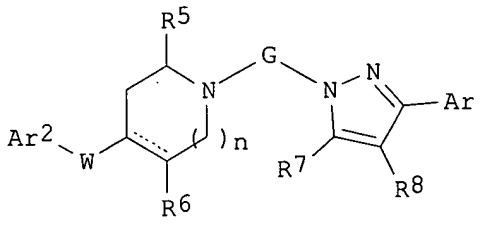
L15 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:184898 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 136:247575
TITLE: Preparation of 3-phenyl-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridines as cathepsin S inhibitors for treating allergies
INVENTOR(S): Butler, Christopher R.; ***Cai, Hui***; ***Edwards, James P.***; Grice, Cheryl A.; Gu, Yin; Gustin, Darin J.; Karlsson, Lars; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Sehon, Clark A.; Sun, Siquan; Tays, Kevin L.; Thurmond, Robin L.; Wei, Jianmei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020011	A2	20020314	WO 2001-US27429	20010905
WO 2002020011	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003078419	A1	20030424	US 2001-927324	20010810

US 6953793	B2	20051011			
CA 2421493	AA	20020314	CA 2001-2421493		20010905
AU 2001088706	A5	20020322	AU 2001-88706		20010905
EP 1315490	A2	20030604	EP 2001-968461		20010905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001014054	A	20030701	BR 2001-14054		20010905
JP 2004531456	T2	20041014	JP 2002-524495		20010905
NZ 524681	A	20050930	NZ 2001-524681		20010905
PRIORITY APPLN. INFO.:			US 2000-230407P	P	20000906
			US 2001-927324	A	20010810
			US 2000-225178P	P	20000814
			WO 2001-US27429	W	20010905

OTHER SOURCE(S): MARPAT 136:247575

GI



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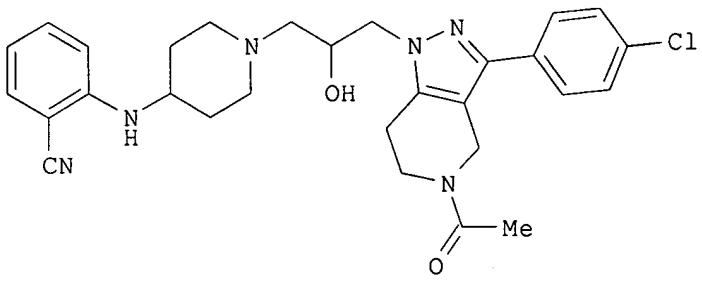

II

AB Title compds. I [wherein Ar and Ar2 = independently (un)substituted mono- or bicyclic (hetero)aryl; G = (un)substituted alkenediyl or alkanediyl; W = O, S, (un)substituted N or CH, CO, CONH, NHCO, or a bond; R5 and R6 = independently H or alkyl; R7 and R8 = independently H, alkyl, alkenyl, alkoxy, alkylthio, halo, or (un)substituted carbocyclyl or heterocyclyl; or R7R8 form an (un)substituted carbocyclic or heterocyclic ring; Rz = H, OH, or is absent; n = 0-2; or pharmaceutically acceptable salts, amides, esters, or stereoisomers thereof] were prepared as cathepsin S inhibitors for the treatment of an allergic condition, including an atopic allergic conditions. For example, N-acetyl-4-piperidone was condensed with morpholine in the presence of TsOH to give the enamine. Reaction with 4-ClC6H4COCl and cycloaddn. of the product with H2NNH2 gave 1-[3-(4-chlorophenyl)-1,4,6,7-tetrahydropyrazolo[4,3-c]pyridin-5-yl]ethanone (42%). Alkylation with epichlorohydrin (60%), followed by addition of 1,4-dioxa-8-azaspiro[4.5]decane (81%), conversion to the piperidinone (65%), and reductive addition of 2-aminobenzonitrile (20%), afforded II. The latter inhibited recombinant human cathepsin S with IC50

of 0.73 μM.

L15 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:142709 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 136:200183
TITLE: Substituted and/or fused pyrazoles, particularly indolylpiperidinylpropyl-substituted pyrazolopyridines, useful as cathepsin S inhibitors, and their pharmaceutical compositions and use as immunosuppressants
INVENTOR(S): ***Cai, Hui; Edwards, James P.;*** Meduna, Steven P.; Pio, Barbara A.; Wei, Jianmei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014317	A2	20020221	WO 2001-US25180	20010810
WO 2002014317	A3	20020704		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2419550	AA	20020221	CA 2001-2419550	20010810
AU 2001084823	A5	20020225	AU 2001-84823	20010810
US 2002040019	A1	20020404	US 2001-927188	20010810
US 6635633	B2	20031021		
EP 1309592	A2	20030514	EP 2001-963912	20010810
EP 1309592	B1	20060426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004512273	T2	20040422	JP 2002-519457	20010810
NZ 524192	A	20050225	NZ 2001-524192	20010810
AT 324372	E	20060515	AT 2001-963912	20010810
RU 2278863	C2	20060627	RU 2003-107014	20010810
ZA 2003002051	A	20040625	ZA 2003-2051	20030313
ZA 2003002056	A	20040702	ZA 2003-2056	20030313
US 2003225062	A1	20031204	US 2003-402694	20030328
US 6936603	B2	20050830		
US 2003225063	A1	20031204	US 2003-402696	20030328
US 6951851	B2	20051004		
US 2003229075	A1	20031211	US 2003-401486	20030328
US 6949540	B2	20050927		
US 2004044027	A1	20040304	US 2003-638032	20030808
US 2005234102	A1	20051020	US 2005-147923	20050608

PRIORITY APPLN. INFO.:			
	US 2000-225178P	P	20000814
	US 2001-927188	A	20010810
	WO 2001-US25180	W	20010810
	US 2003-401486	A1	20030328

OTHER SOURCE(S): MARPAT 136:200183
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Substituted pyrazoles I, methods of manufacturing them, compns. containing them, and methods of using them to treat, for example, autoimmune diseases mediated by cathepsin S, are described [W, X, Y, Z = N, (un)substituted CH (0-3 of them may be N; or 1 can be N-oxide when other 3 ≠ N); R = H, alkyl, cyano, hydroxyalkyl, acyl, CHO, alkoxycarbonyl, or (un)substituted carbamoyl; R1, R2 = H, alkyl; R3, R4 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, or 4- to 7-membered carbo- or heterocyclyl; or R3R4 = atoms to form (un)substituted (un)saturated (non)aromatic 5- to 7-membered carbo- or heterocyclic ring; Ar = (un)substituted mono- or bicyclic (hetero)aryl; n = 0-2; G = (un)substituted C3-6 alkanediyl or alkenediyl (substituents = OH, halo, oxo, aminoalkyl, etc.); Q = O, S, (un)substituted NH; including stereoisomers, pharmaceutically acceptable salts, esters, and amides]. Claimed uses include treatment of lupus, rheumatoid arthritis, and particularly asthma, and inhibition of tissue transplant rejection. Approx. 70 individual compds. I were prepared and/or claimed, with detailed prepns. given for 13 compds. For instance, 6-(morpholin-4-yl)-3-(piperidin-4-yl)-1H-pyrrolo[3,2-c]pyridine (prepared in 5 steps) reacted with the corresponding epoxide (prepared in several steps) to give title compound II, a preferred compound In an assay for inhibition of recombinant human cathepsin S in vitro, II had an IC50 of 0.02 μM. Compound III is another one of four specifically preferred compds.

L15 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:142708 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 136:200182
TITLE: Substituted and/or fused pyrazoles, particularly piperidinylpropyl-substituted pyrazolopyridines, useful as cathepsin S inhibitors, and their pharmaceutical compositions and use as immunosuppressants
INVENTOR(S): Butler, Christopher R.; ***Cai, Hui***; ***Edwards, James P.***; Grice, Cheryl A.; Gustin, Darin J.; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Sehon, Clark A.; Tays, Kevin L.; Wei, Jianmei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 235 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014315	A2	20020221	WO 2001-US25290	20010810
WO 2002014315	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2419552	AA	20020221	CA 2001-2419552	20010810
AU 2001086454	A5	20020225	AU 2001-86454	20010810
US 2003078419	A1	20030424	US 2001-927324	20010810
US 6953793	B2	20051011		
EP 1309593	A2	20030514	EP 2001-965898	20010810
EP 1309593	B1	20060315		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001013286	A	20030909	BR 2001-13286	20010810
JP 2004511440	T2	20040415	JP 2002-519455	20010810
NZ 524191	A	20041126	NZ 2001-524191	20010810
AT 320427	E	20060415	AT 2001-965898	20010810
ZA 2003002051	A	20040625	ZA 2003-2051	20030313
ZA 2003002056	A	20040702	ZA 2003-2056	20030313
US 2005234102	A1	20051020	US 2005-147923	20050608
US 2005245576	A1	20051103	US 2005-174077	20050630

PRIORITY APPLN. INFO.:

US 2000-225178P	P	20000814
US 2001-927324	A	20010810
US 2001-927188	A3	20010810
WO 2001-US25290	W	20010810
US 2003-401486	A1	20030328

OTHER SOURCE(S): MARPAT 136:200182
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Substituted pyrazoles I, methods of manufacturing them, compns. containing them, and
methods of using them to treat, for example, autoimmune diseases mediated by cathepsin S, are described [R = H, OH, or absent; R1, R2 = H, alkyl; R3, R4 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, or 4- to 7-membered carbo- or heterocyclyl; or R3R4 = atoms to form (un)substituted (un)saturated (non)aromatic 5- to 7-membered carbo- or heterocyclic ring; Ar1 = (un)substituted mono- or bicyclic (hetero)aryl; Ar2 = (un)substituted (un)saturated (non)aromatic mono- or bicyclic ring system with 0-5 heteroat. ring
moieties selected from O, S, N, SO2, and CO; n = 0-2; G = (un)substituted C3-6 alkanediyl or alkenediyl (substituents = OH, halo, oxo, aminoalkyl, etc.); W = O, S, CO CONH, NHCO, (un)substituted NH or CH2; including stereoisomers, pharmaceutically acceptable salts, esters, and amides]. Claimed usages include treatment of lupus, rheumatoid arthritis, and particularly asthma, and inhibition of tissue transplant rejection. Approx. 350 individual compds. I were prepared and/or claimed, with detailed prepns. given for 31 compds. For instance, 6-chloro-1-(piperidin-4-yl)-3,4-dihydro-1H-quinolin-2-one (prepared in 6 steps) reacted with the corresponding epoxide (prepared in several steps) to give title compound II. In an assay for inhibition of recombinant human cathepsin S in vitro, II had an IC50 of 0.01 μM. Compound III is one of two specifically preferred compds.

L15 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:142707 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 136:200181
TITLE: Substituted and/or fused pyrazoles, particularly piperazinylpropyl-substituted pyrazolopyridines, useful as cathepsin S inhibitors, and their pharmaceutical compositions and use as immunosuppressants
INVENTOR(S): Breitenbucher, J. Guy; ***Cai, Hui***; ***Edwards, James P.***; Grice, Cheryl A.; Gustin, Darin J.; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Tays, Kevin L.; Wei, Jianmei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014314	A2	20020221	WO 2001-US25289	20010810
WO 2002014314	A3	20020606		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2419540	AA	20020221	CA 2001-2419540	20010810
AU 2001081255	A5	20020225	AU 2001-81255	20010810
US 2002040020	A1	20020404	US 2001-928122	20010810
EP 1309591	A2	20030514	EP 2001-959731	20010810
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004512272	T2	20040422	JP 2002-519454	20010810
NZ 524193	A	20041224	NZ 2001-524193	20010810
ZA 2003002052	A	20040623	ZA 2003-2052	20030313

PRIORITY APPLN. INFO.:			
	US 2000-225138P	P	20000814
	US 2001-928122	A	20010810
	WO 2001-US25289	W	20010810

OTHER SOURCE(S): MARPAT 136:200181
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Substituted pyrazoles I, methods of manufacturing them, compns. containing them, and
methods of using them to treat, for example, autoimmune diseases mediated by cathepsin S, are described [R1 = H, N3, halo, alkoxy, OH, alkyl, alkenyl, cyano, NO2, (un)substituted NH2, acyl, etc.; R2 = H, halo,

alkoxy, alkyl, alkenyl, haloalkyl, cyano, or (un)substituted NH2; or R1R2 = atoms to form (un)substituted (un)saturated (non)aromatic 5- to 7-membered carbo- or heterocyclic ring; R3, R4 = H, alkyl; R5, R6 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, or 4- to 7-membered carbo- or heterocyclyl; or R5R6 = atoms to form (un)substituted (un)saturated (non)aromatic 5- to 7-membered carbo- or heterocyclic ring; n = 1 or 2; G = (un)substituted C3-6 alkanediyl or alkenediyl (substituents = OH, halo, oxo, aminoalkyl, etc.); X, Y, Z = N, (un)substituted CH; Ar = (un)substituted mono- or bicyclic (hetero)aryl; W = SO2, CO, (un)substituted CH2, bond; or WR1 = atoms to form a benzoxazol-2-yl, benzothiazol-2-yl, benzimidazol-2-yl, 1,2-benzisoxazol-3-yl, 1,2-benzisothiazol-3-yl, or 1,1-dioxo-1,2-benzothiazol-3-yl ring; including stereoisomers and pharmaceutically acceptable salts, esters, and amides]. Claimed usages include treatment of lupus, rheumatoid arthritis, and particularly asthma, and inhibition of tissue transplant rejection. Approx. 250 individual compds. I were prepared and/or claimed, with detailed prepns. given for 24 compds. For instance, 4-(2-chloro-6-methanesulfonylaminophenyl)piperazine-1-carboxylic acid tert-Bu ester (prepared in 4 steps) was deprotected with TFA and coupled with the corresponding epoxide (prepared in several steps) to give title compound II, a preferred compound In an assay for inhibition of recombinant human cathepsin S in vitro, II had an IC50 of 0.06 μM. Compound III was another of three specifically preferred compds.

L15 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:122980 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER: 136:183708
TITLE: Preparation of non-imidazole aryloxyalkylamines as histamine H3 receptor antagonists
INVENTOR(S): Apodaca, Richard; ***Carruthers, Nicholas I.***; ***Dvorak, Curt A.***; Rudolph, Dale A.; Shah, Chandravadan R.; Xiao, Wei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical Inc., USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012214	A2	20020214	WO 2001-US24655	20010806
WO 2002012214	A3	20020620		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2418369	AA	20020214	CA 2001-2418369	20010806
AU 2001084733	A5	20020218	AU 2001-84733	20010806
US 2002065278	A1	20020530	US 2001-922631	20010806
EP 1313721	A2	20030528	EP 2001-963813	20010806
EP 1313721	B1	20060308		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004505960	T2	20040226	JP 2002-518191		20010806
BR 2001013162	A	20040406	BR 2001-13162		20010806
ZA 2003001853	A	20040621	ZA 2003-1853		20030306
ZA 2003001854	A	20040621	ZA 2003-1854		20030306
PRIORITY APPLN. INFO.:			US 2000-223768P	P	20000808
			US 2001-922631	A	20010806
			WO 2001-US24655	W	20010806

OTHER SOURCE(S): MARPAT 136:183708

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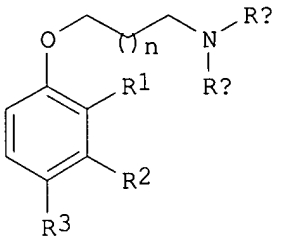

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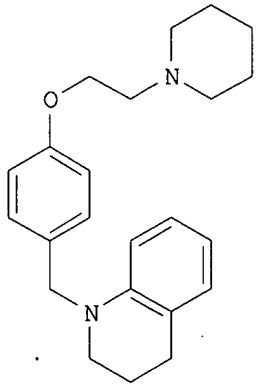


II

AB Title compds. I [Ra-b = alk(en/yn)yl, cycloalkyl; n = 0-4; one of R1-3 = G and the remaining two are H or halo; G = N-containing heterocycle, e.g., piperidinyl, etc.] were prepared For instance, 4-(2-(piperidin-1-yl)ethoxy)benzaldehyde was used to alkylate 1,2,3,4-tetrahydroisoquinoline (ClCH2CH2Cl, HOAc, NaBH(OAc)3, 15 h) to give II. II had Ki = 37 nM for the histamine H3 receptor. I are useful for treating histamine-mediated conditions.

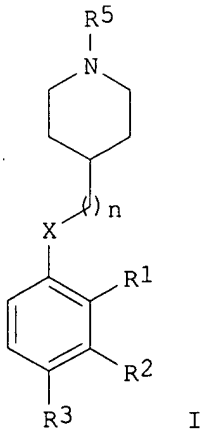
L15 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2002:122957 HCAPLUS <<LOGINID::20060731>>
DOCUMENT NUMBER:	136:167285
TITLE:	Preparation of aryloxypiperidines as histamine H3 receptor antagonists
INVENTOR(S):	Apodaca, Richard; ***Carruthers, Nicholas I.***; ***Dvorak, Curt A.***; Shah, Chandravadan R.; Xiao, Wei

PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002012190	A2	20020214	WO 2001-US24660		20010806
WO 2002012190	A3	20020801			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2419036	AA	20020214	CA 2001-2419036		20010806
AU 2001081121	A5	20020218	AU 2001-81121		20010806
US 2002040024	A1	20020404	US 2001-922619		20010806
US 7071191	B2	20060704			
EP 1311482	A2	20030521	EP 2001-959582		20010806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001013161	A	20040406	BR 2001-13161		20010806
JP 2004511438	T2	20040415	JP 2002-518168		20010806
ZA 2003001853	A	20040621	ZA 2003-1853		20030306
ZA 2003001854	A	20040621	ZA 2003-1854		20030306
US 2005227979	A1	20051013	US 2005-138631		20050526
PRIORITY APPLN. INFO.:			US 2000-223768P	P	20000808
			US 2001-922619	A	20010806
			WO 2001-US24660	W	20010806

OTHER SOURCE(S): MARPAT 136:167285
GI



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AB Title compds. I [X = O; n = 0-3; R5 = alk(en)yl, cycloalkylalkyl, phenylalk(en)yl, alkylcarbonylalkyl; R1-3 = G, W, wherein one of the remaining two is selected from H and halo and the third being H; G = alk(en/yn)yl-N-containing heterocycle, etc.; W = CN, CHO, halo, heterocyclyl, phenoxy, Ph, etc.] were prepared For example, a suspension of 1-isopropylpiperidin-4-ol (preparation given), 4-fluorobenzaldehyde and Cs2CO3 were heated to 100° in DMF for 22 h resulting in the formation of 4-[(1-isopropylpiperidin-4-yl)oxy]benzaldehyde (II). II had Ki = 36 nM for the histamine H3 receptor. I are useful in the treatment of histamine-mediated conditions.